

#7

1/31

FIG. 1

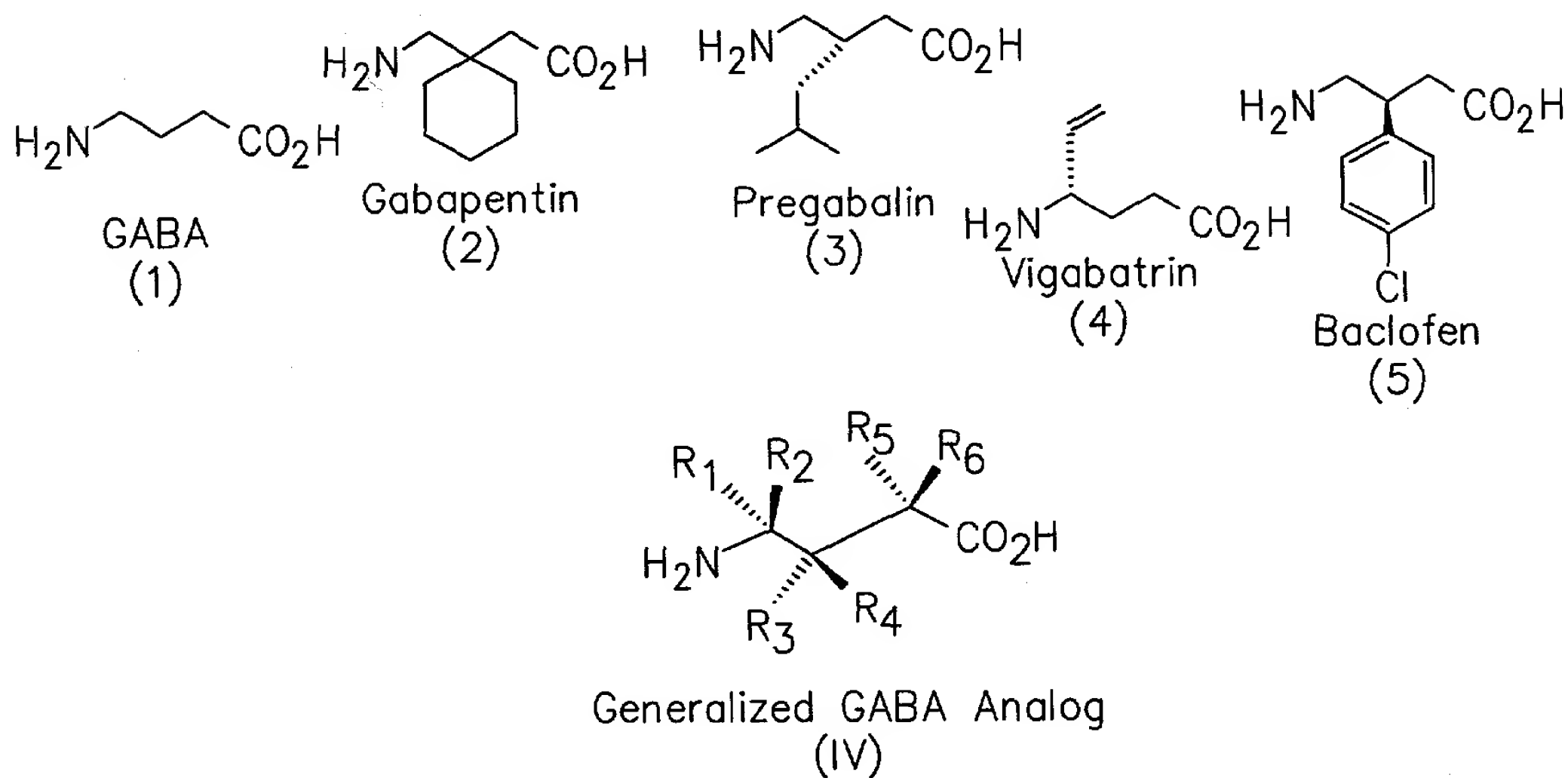
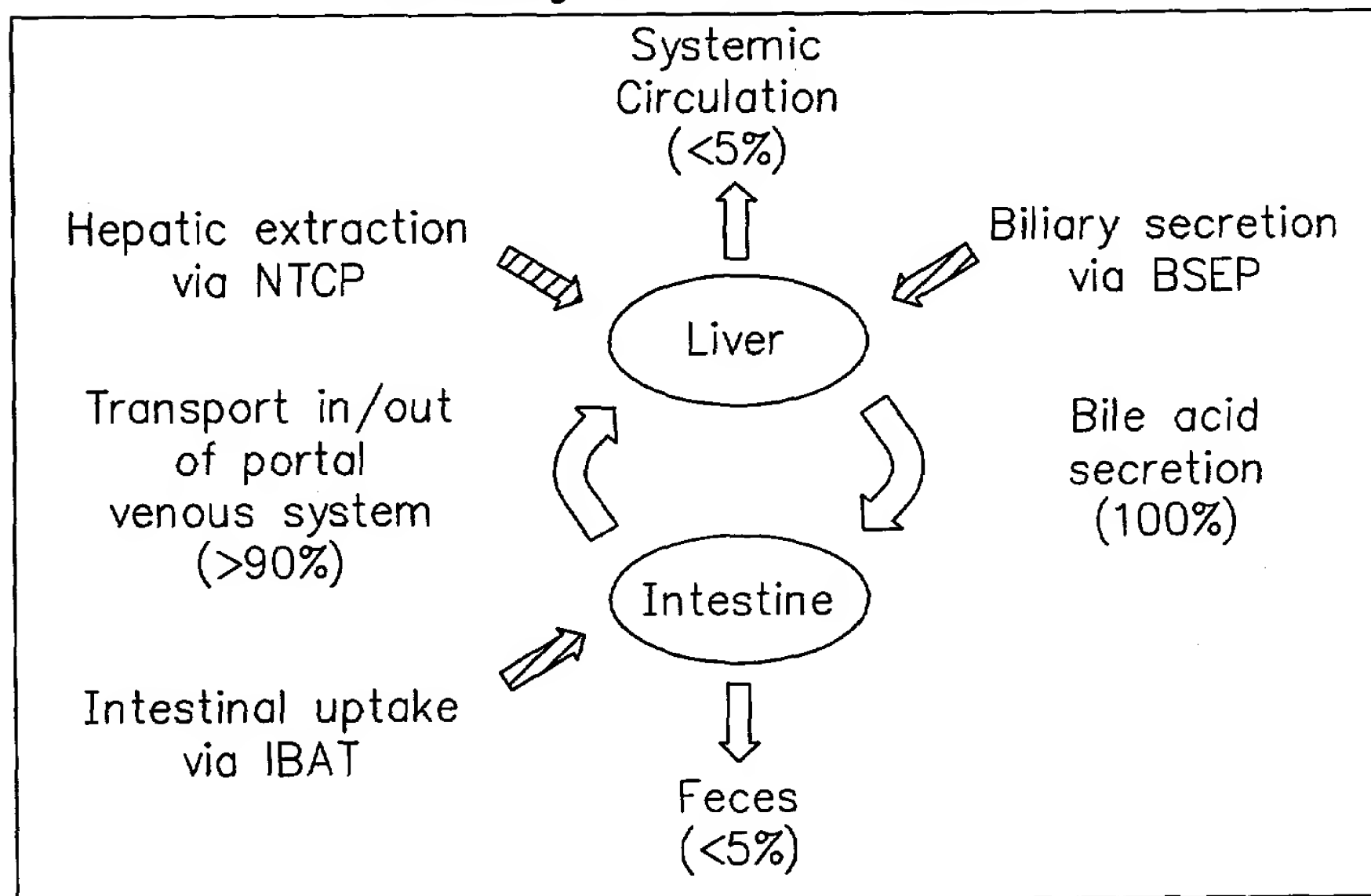


FIG. 2

*The Enterohepatic Circulation with Key Transporter Proteins
Mediating Bile Acid Circulation*



2/31

FIG. 3

Bile Acid Conjugates of HMG-CoA Reductase Inhibitor

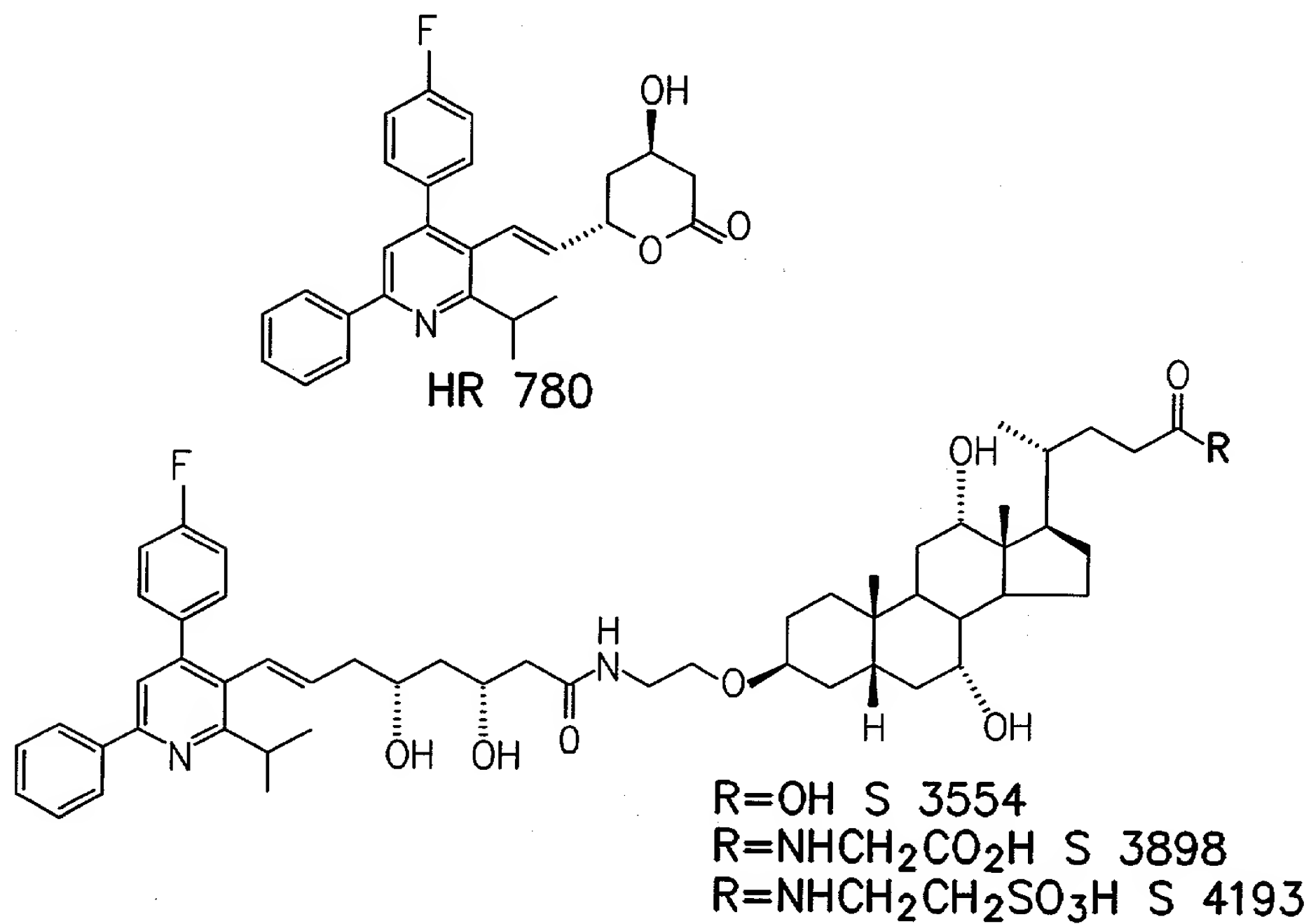
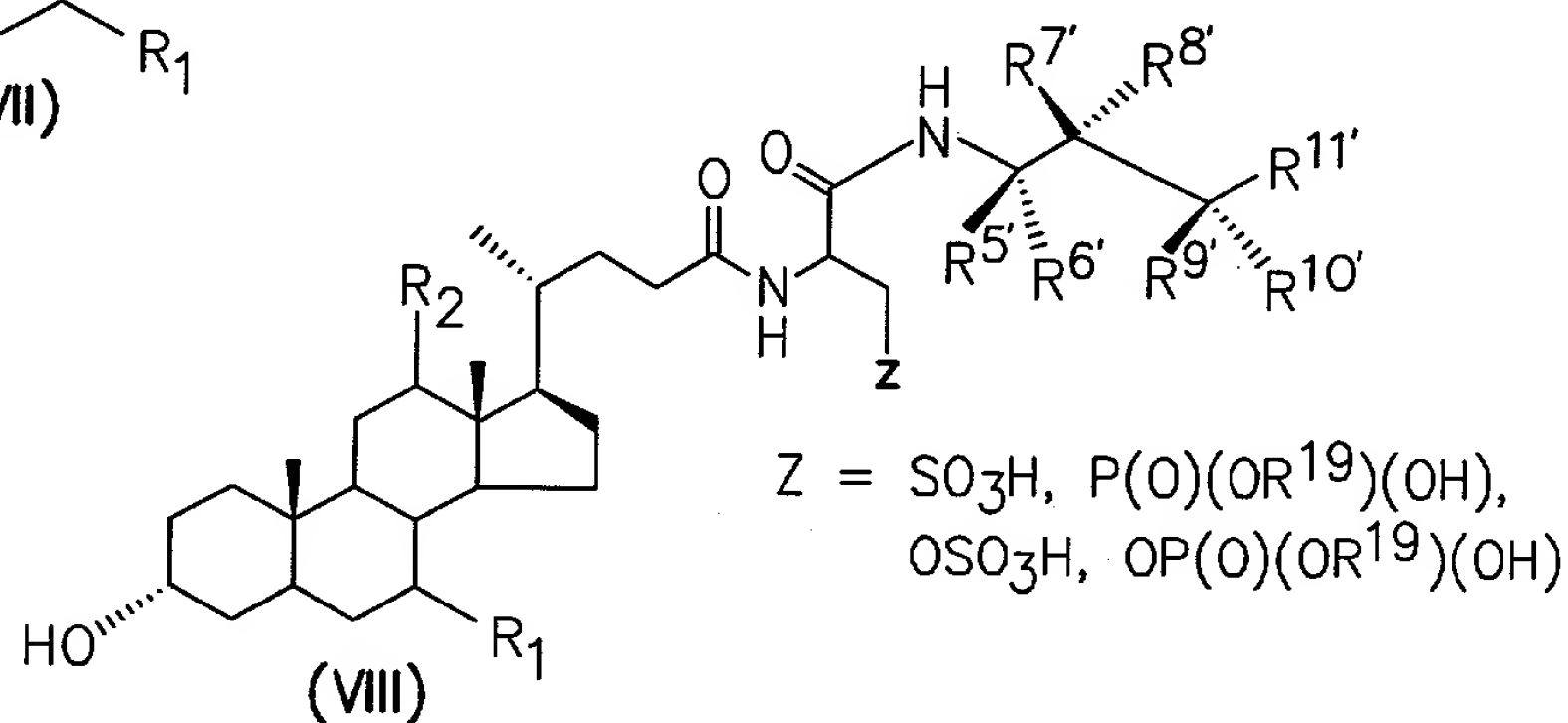
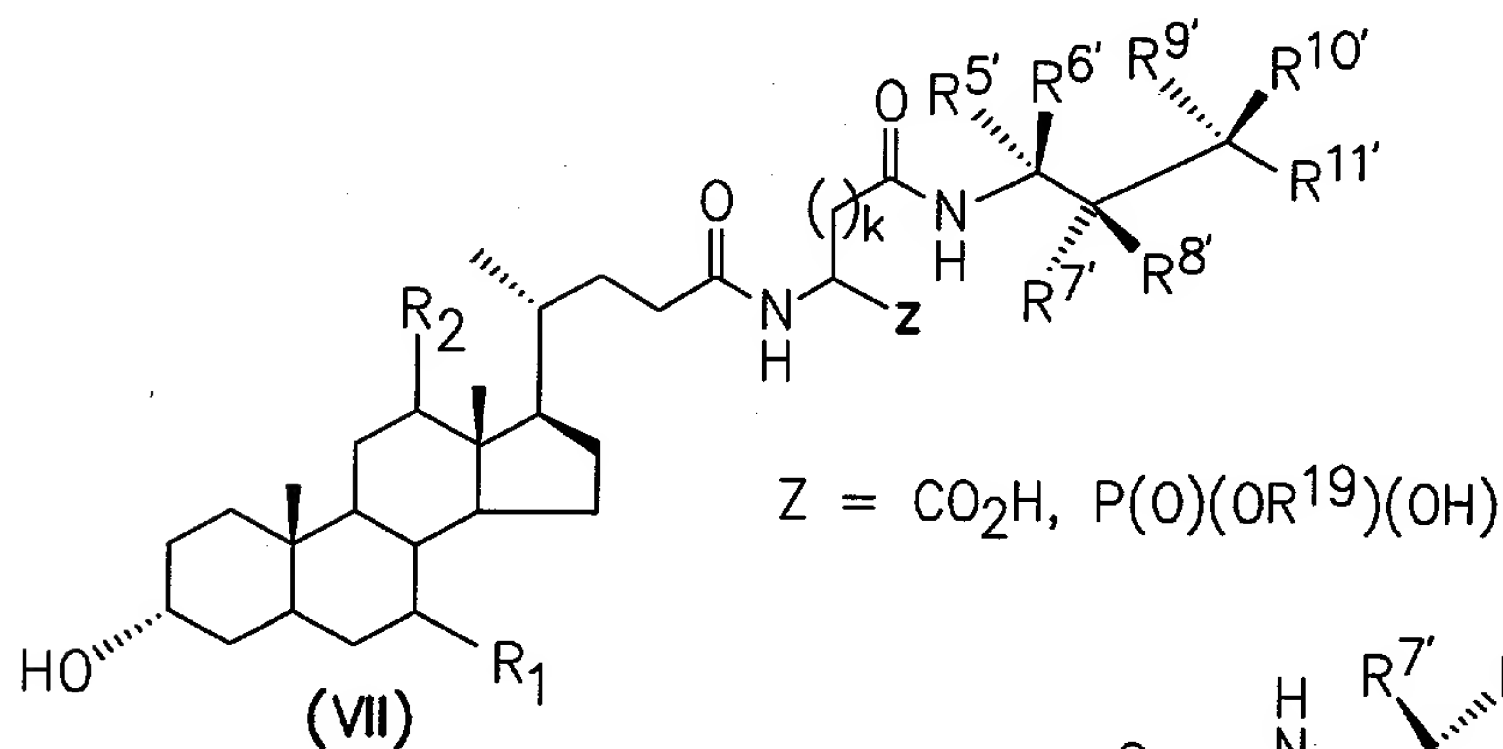
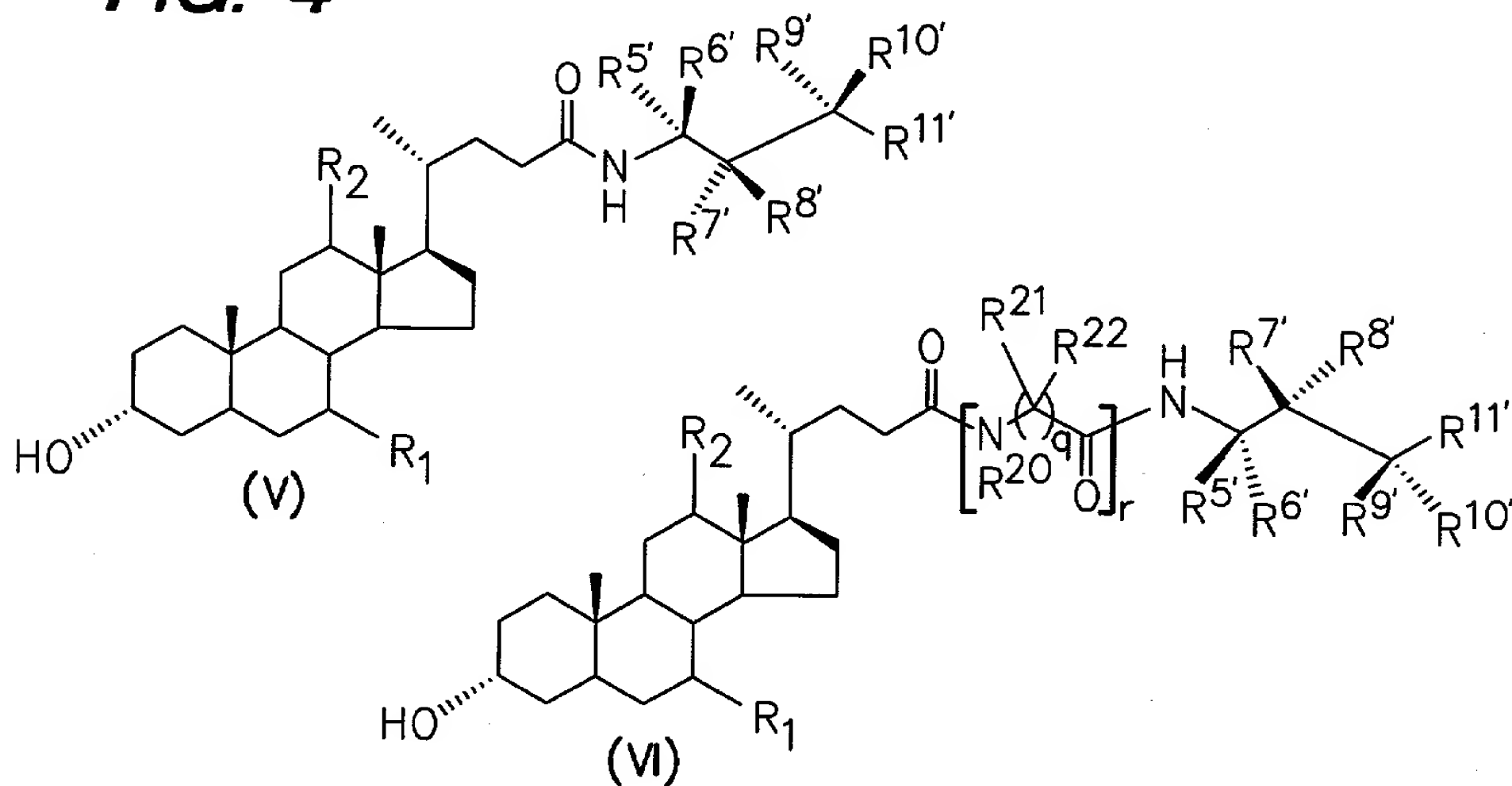


FIG. 4

3/31

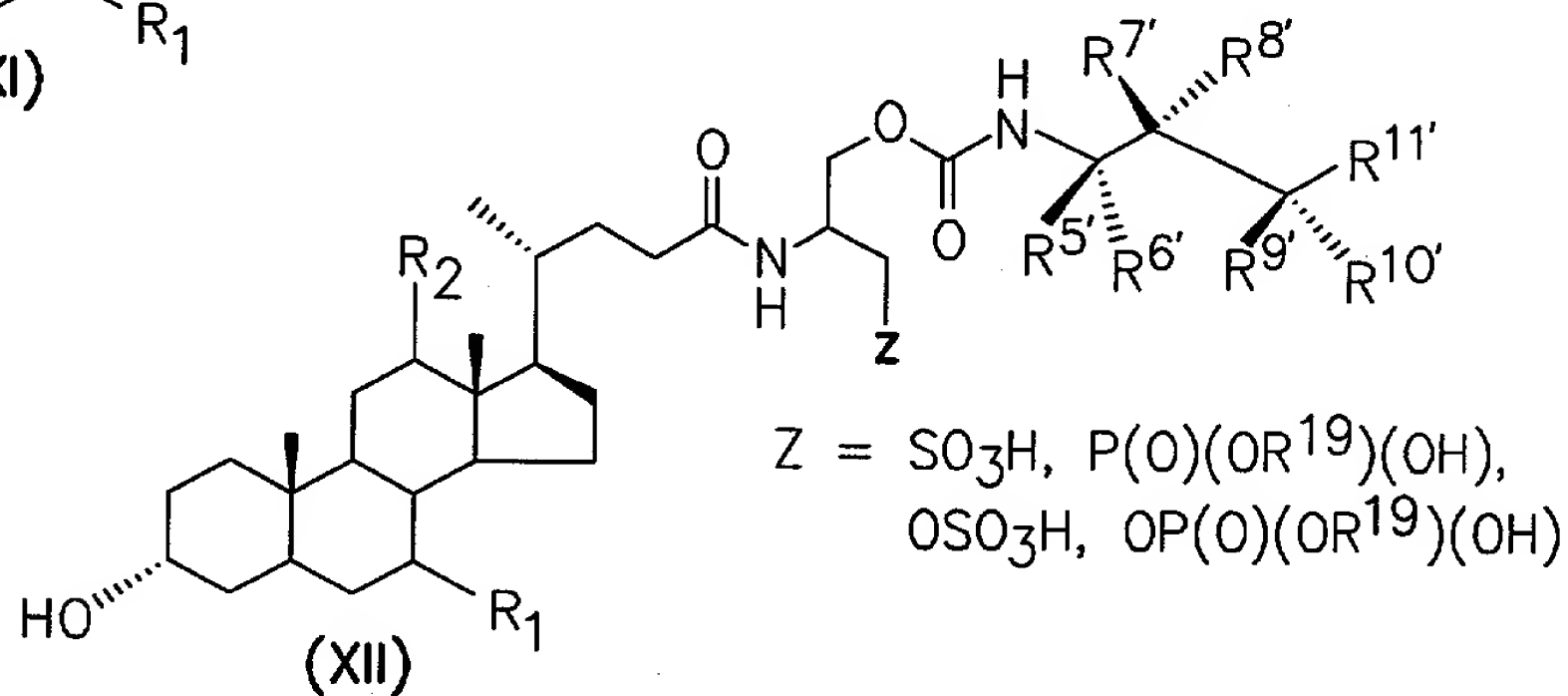
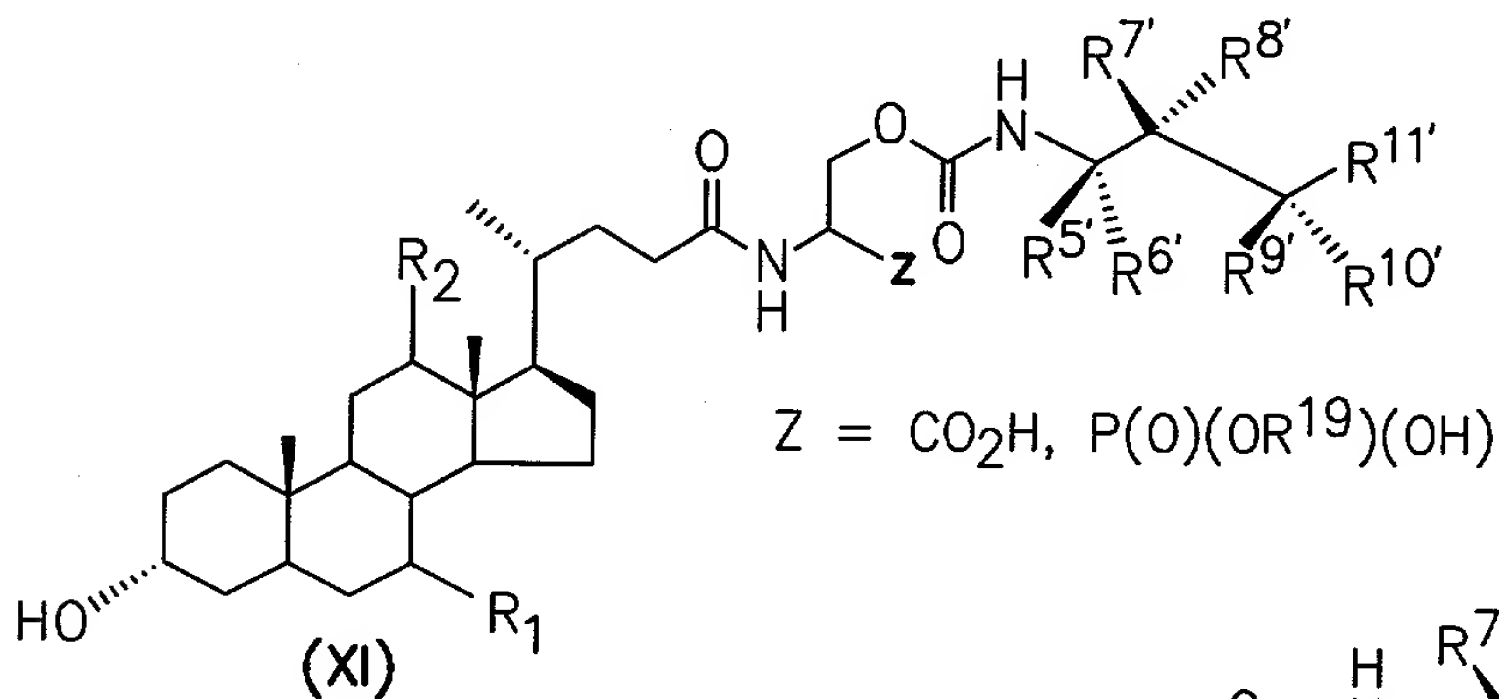
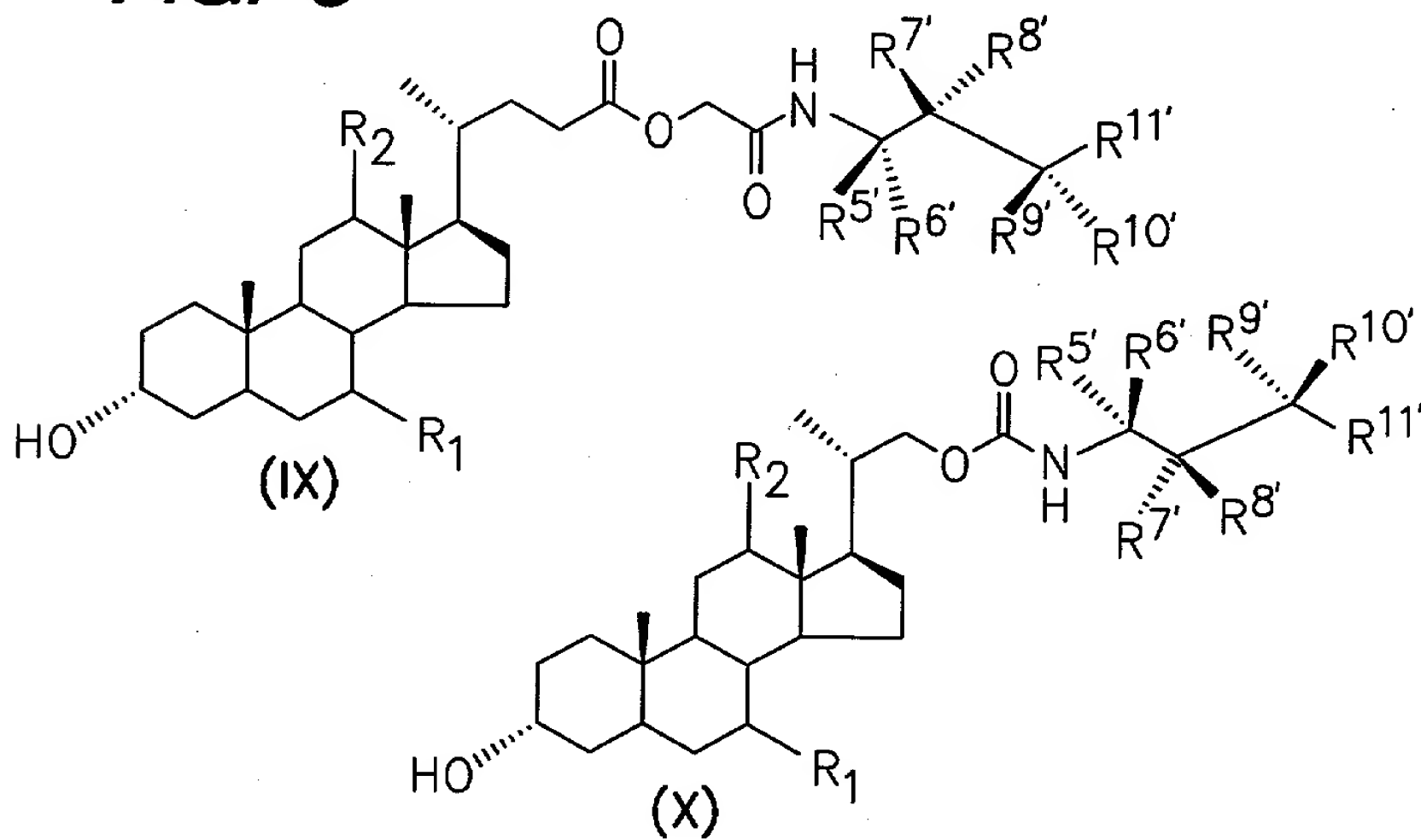


- R₁ = α-OH; R₂ = α-OH (Cholate)
 R₁ = β-OH; R₂ = H (Ursodeoxycholate)
 R₁ = α-OH; R₂ = H (Chenodeoxycholate)
 R₁ = H; R₂ = α-OH (Deoxycholate)
 R₁ = β-OH; R₂ = α-OH (Ursocholate)
 R₁ = H; R₂ = H (Lithocholate)

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FIG. 5

4/31

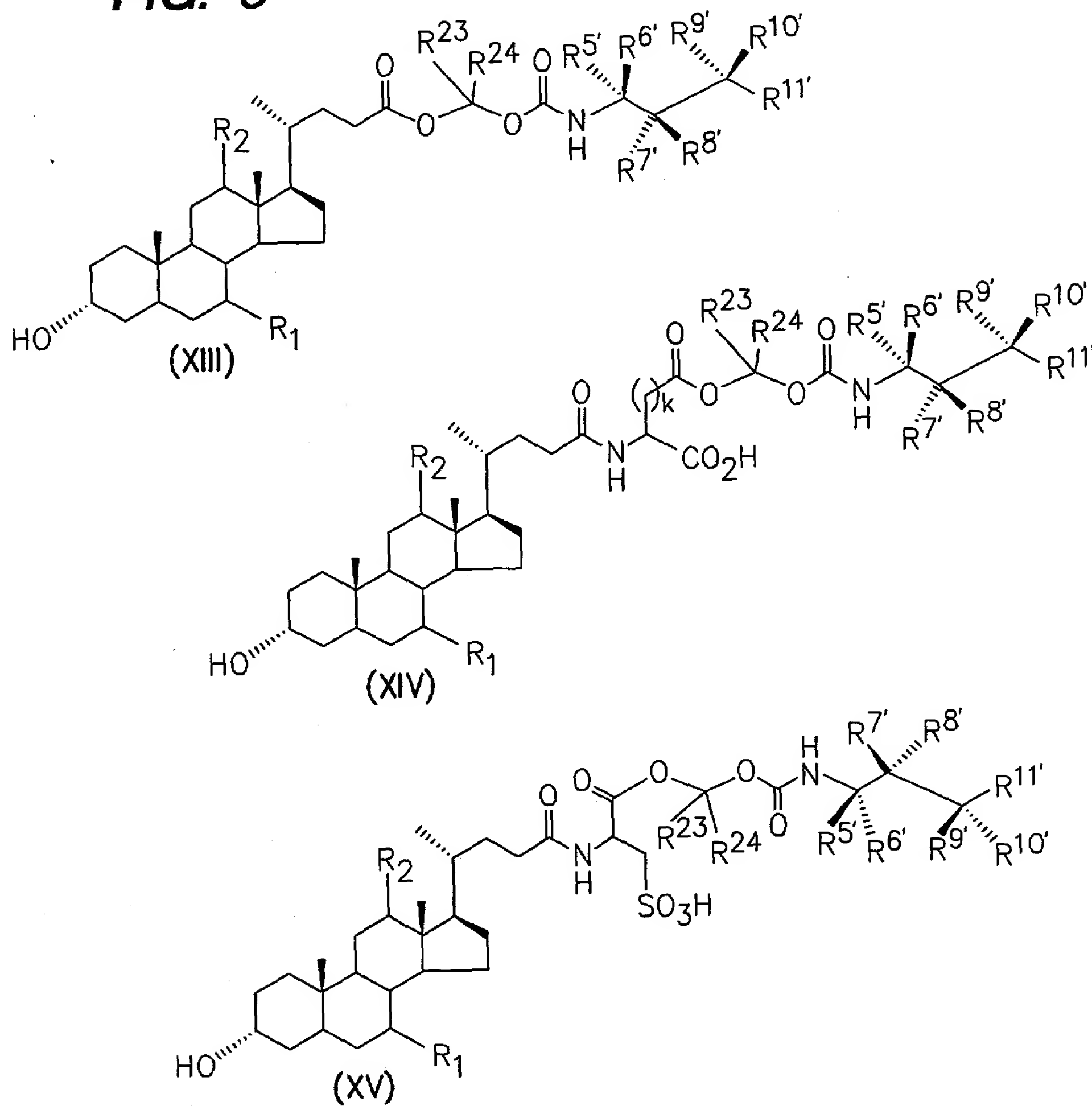


- R1 = α -OH; R2 = α -OH (Cholate)
 R1 = β -OH; R2 = H (Ursodeoxycholate)
 R1 = α -OH; R2 = H (Chenodeoxycholate)
 R1 = H; R2 = α -OH (Deoxycholate)
 R1 = β -OH; R2 = α -OH (Ursocholate)
 R1 = H; R2 = H (Lithocholate)

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5/31

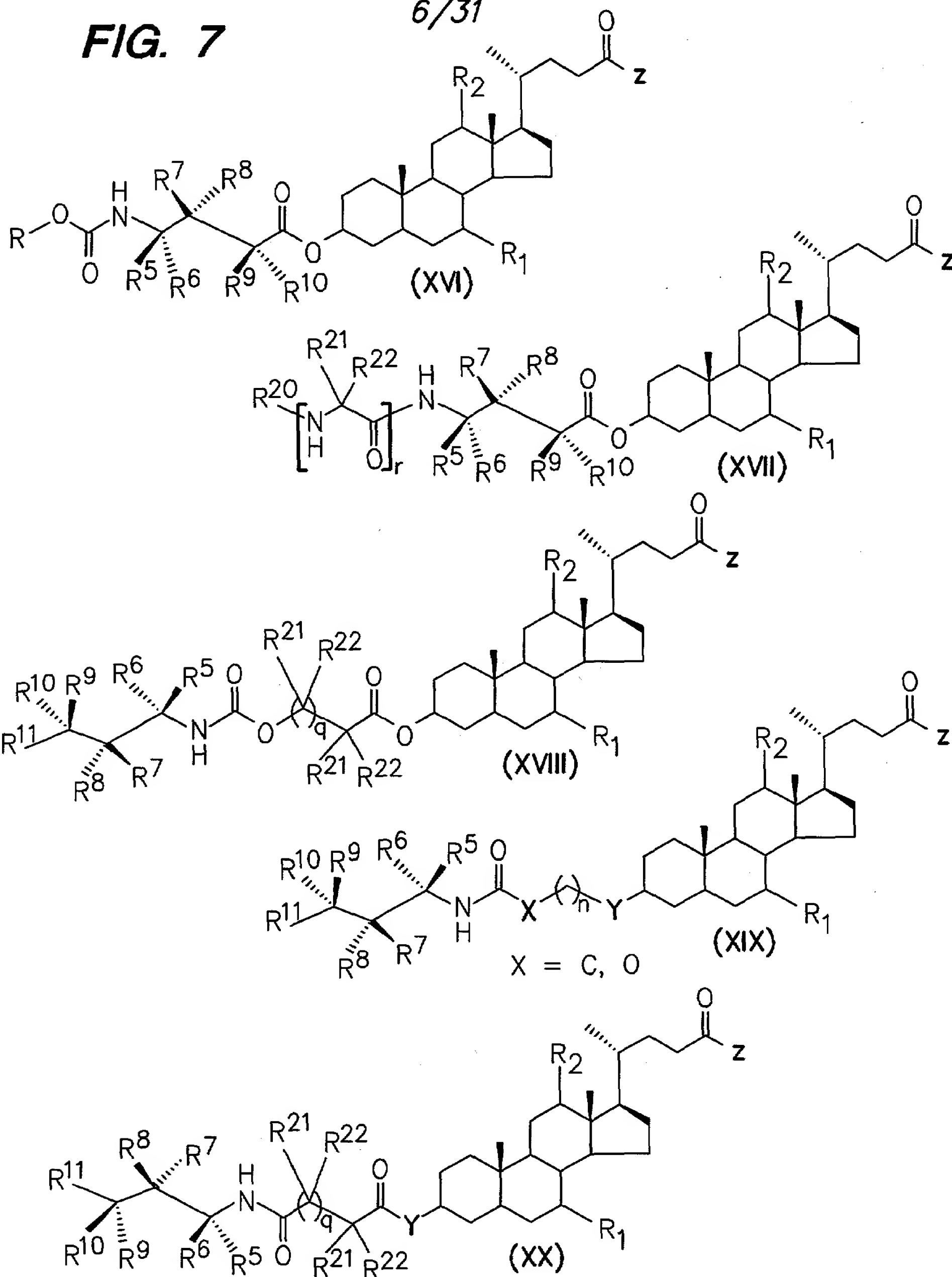
FIG. 6



- R1 = α -OH; R2 = α -OH (Cholate)
 R1 = β -OH; R2 = H (Ursodeoxycholate)
 R1 = α -OH; R2 = H (Chenodeoxycholate)
 R1 = H; R2 = α -OH (Deoxycholate)
 R1 = β -OH; R2 = α -OH (Ursocholate)
 R1 = H; R2 = H (Lithocholate)

FIG. 7

6/31



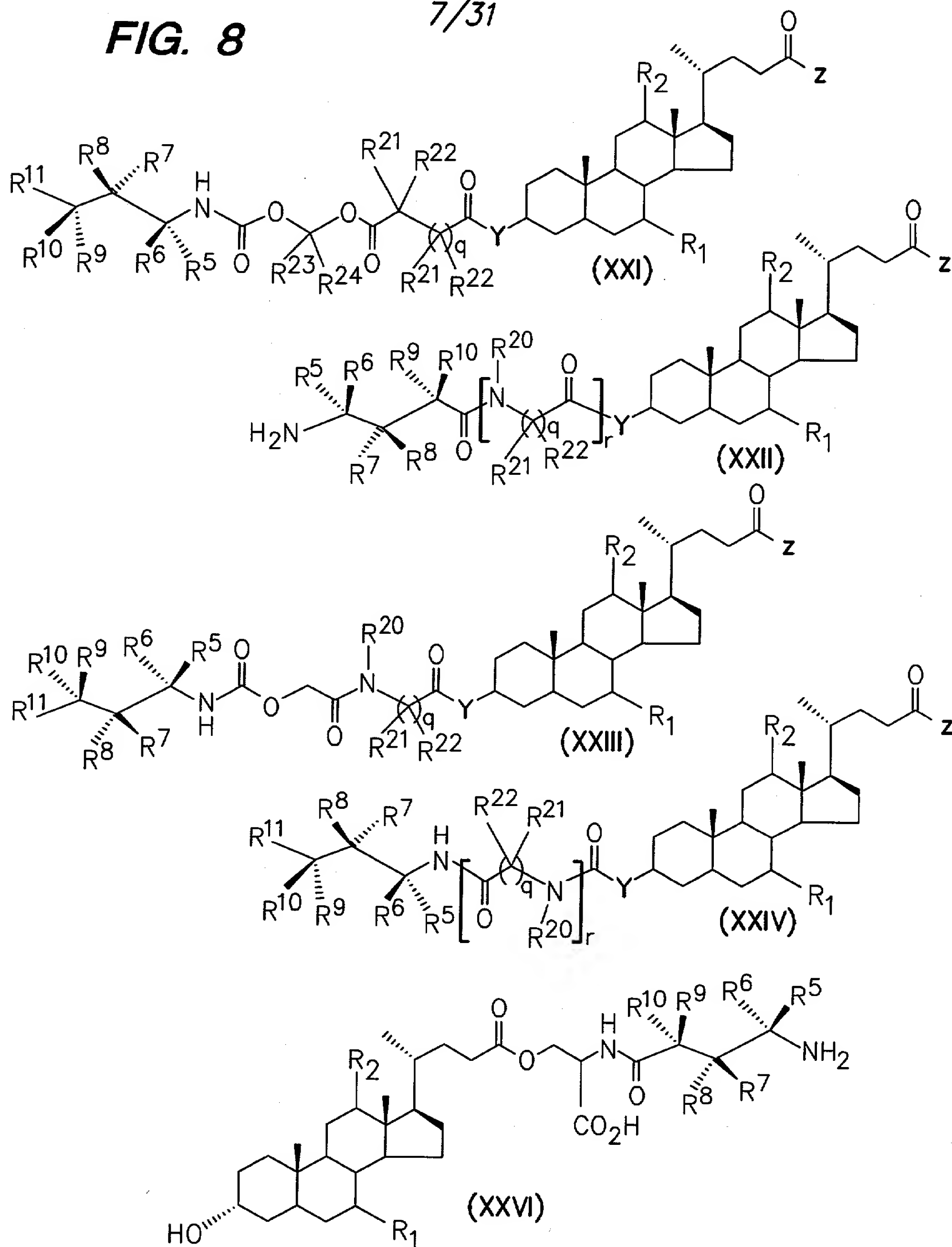
R1 = α -OH; R2 = α -OH (Cholate)
 R1 = β -OH; R2 = H (Ursodeoxycholate)
 R1 = α -OH; R2 = H (Chenodeoxycholate)
 R1 = H; R2 = α -OH (Deoxycholate)
 R1 = β -OH; R2 = α -OH (Ursocholate)
 R1 = H; R2 = H (Lithocholate)

Y = α -O
 Y = β -O
 Y = α -NH
 Y = β -NH

Z = OH
 Z = $\text{N}(\text{H})\text{CH}_2\text{CO}_2\text{H}$
 Z = $\text{N}(\text{H})\text{CH}_2\text{CH}_2\text{SO}_3\text{H}$

FIG. 8

7/31



R₁ = α -OH; R₂ = α -OH (Cholate)
 R₁ = β -OH; R₂ = H (Ursodeoxycholate)
 R₁ = α -OH; R₂ = H (Chenodeoxycholate)
 R₁ = H; R₂ = α -OH (Deoxycholate)
 R₁ = β -OH; R₂ = α -OH (Ursocholate)
 R₁ = H; R₂ = H (Lithocholate)

Y = α -O
 Y = β -O
 Y = α -NH
 Y = β -NH

Z = OH
 Z = N-CH₂-CO₂H
 Z = N-CH₂-SO₃H

8/31

FIG. 9 Uptake of (8) (XP10569) or Glycochocholate by IBAT-Transfected CHO Cells

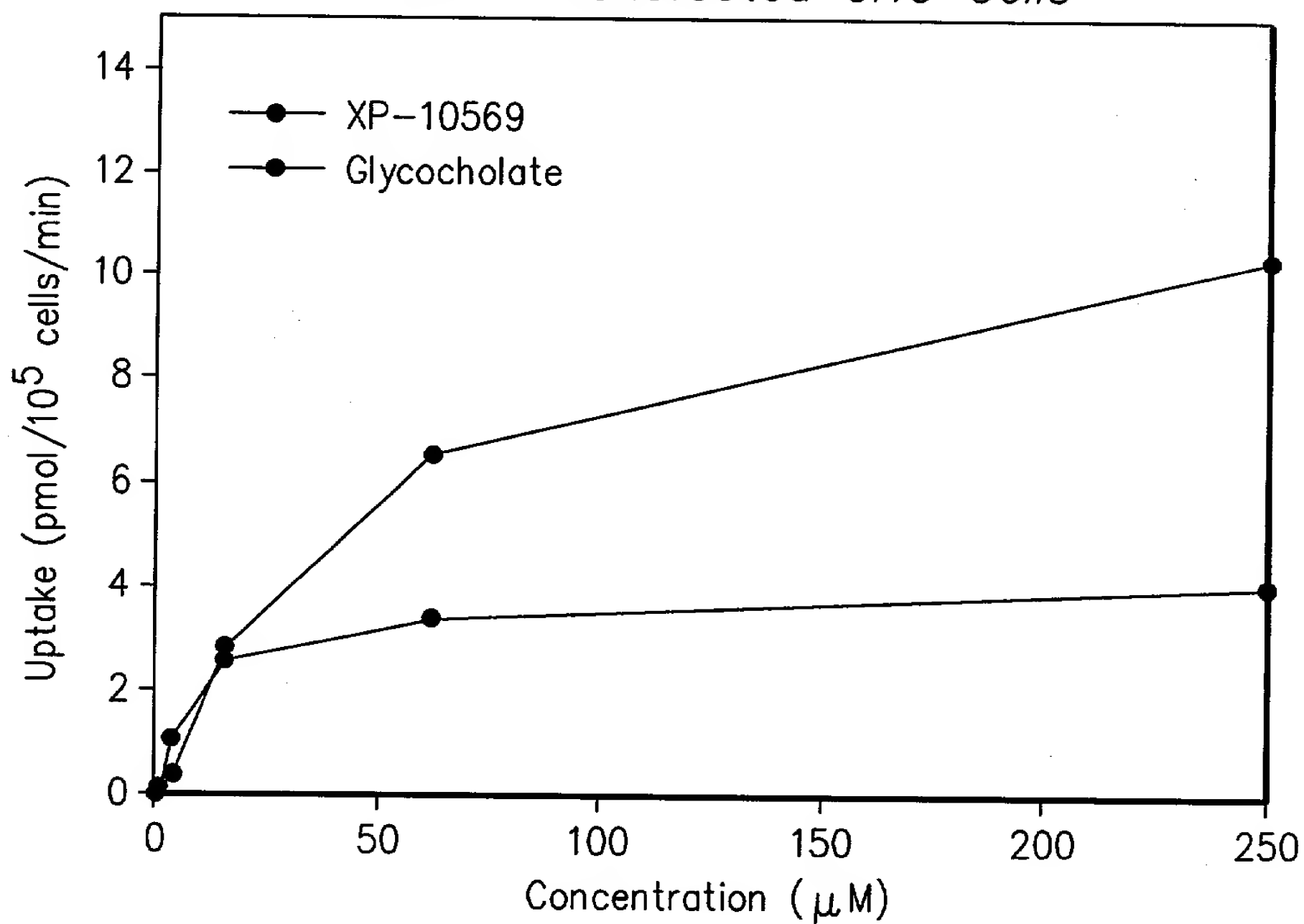


FIG. 10 Uptake of (8) (XP10569) or Glycocholate by LBAT-Transfected CHO Cells

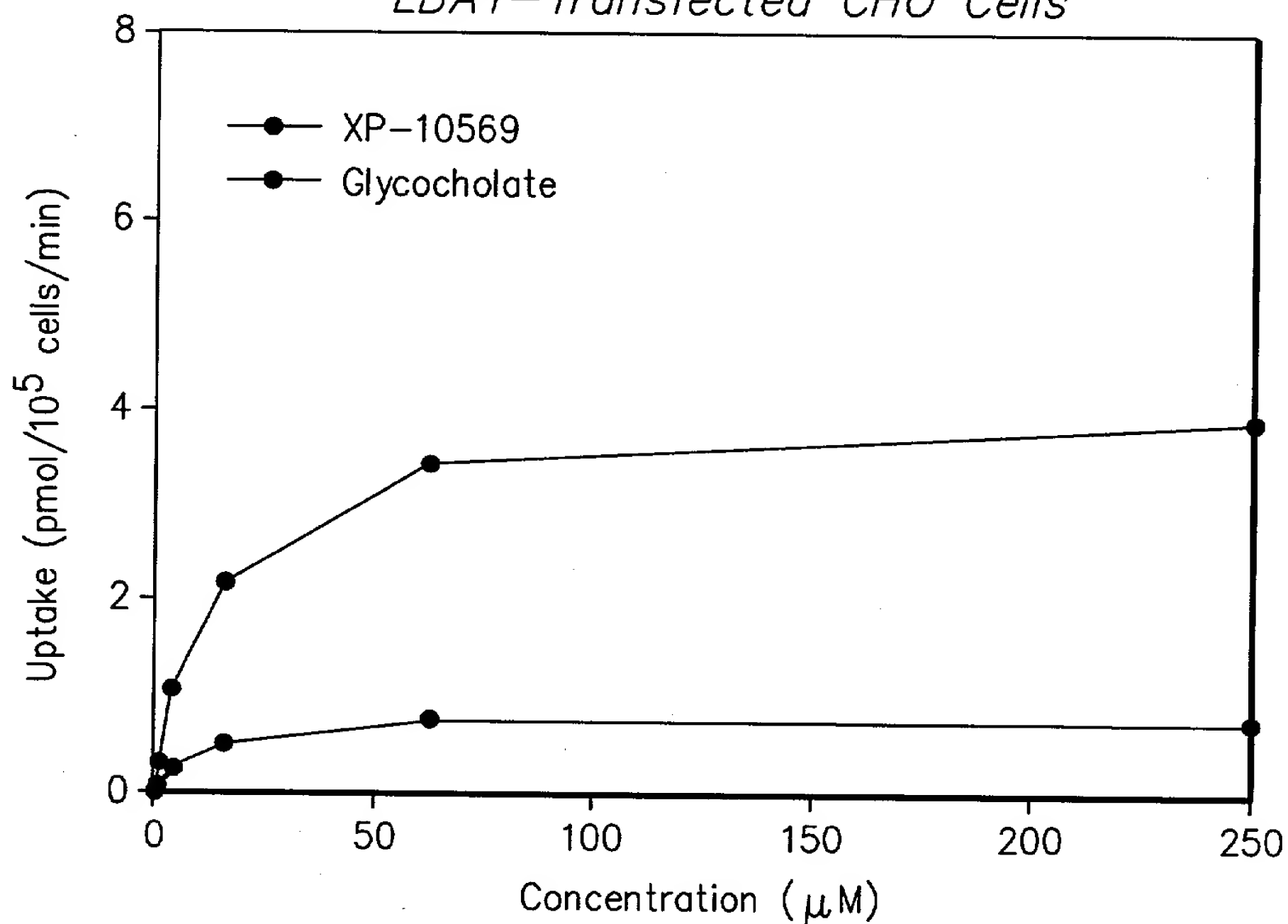
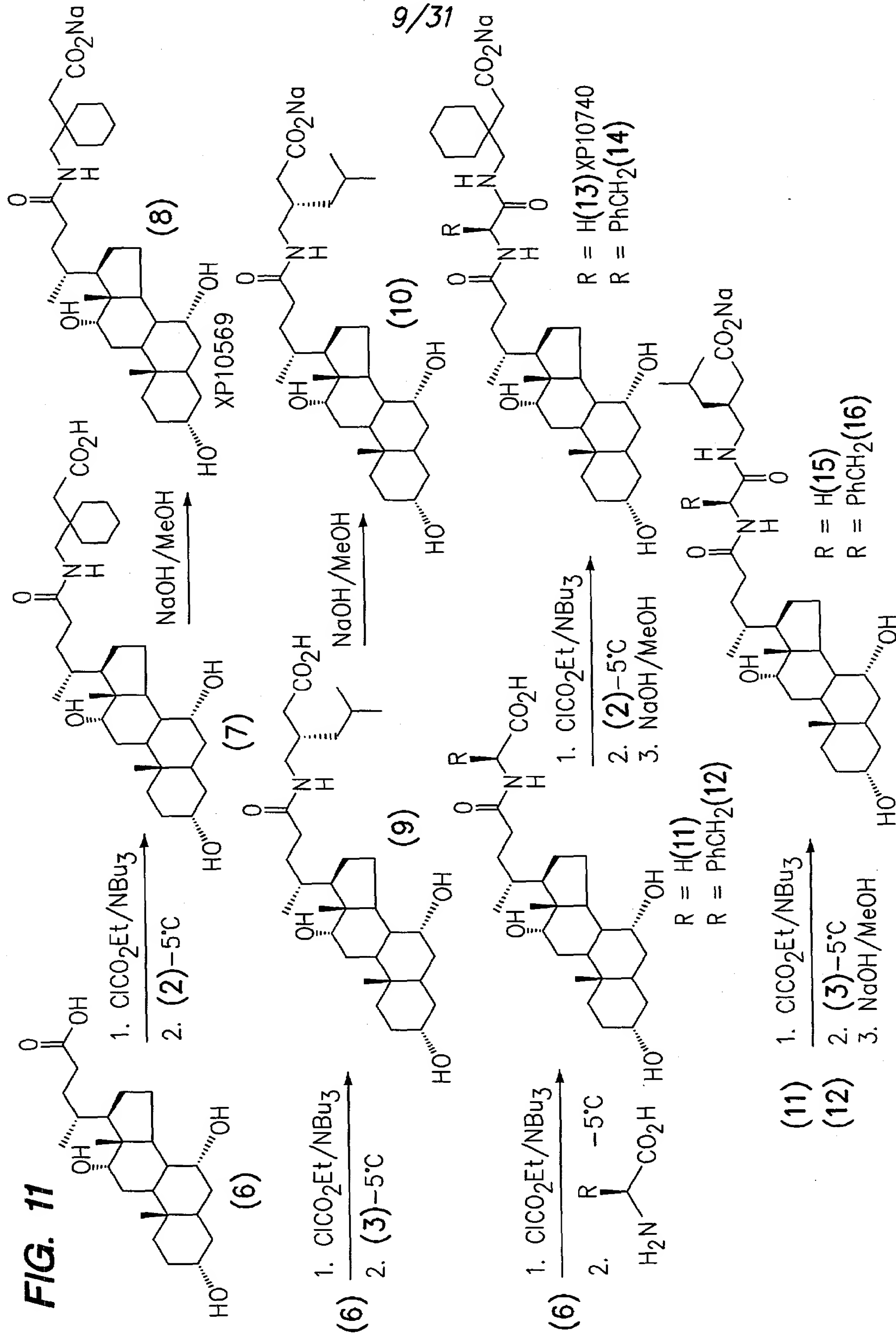


FIG. 11

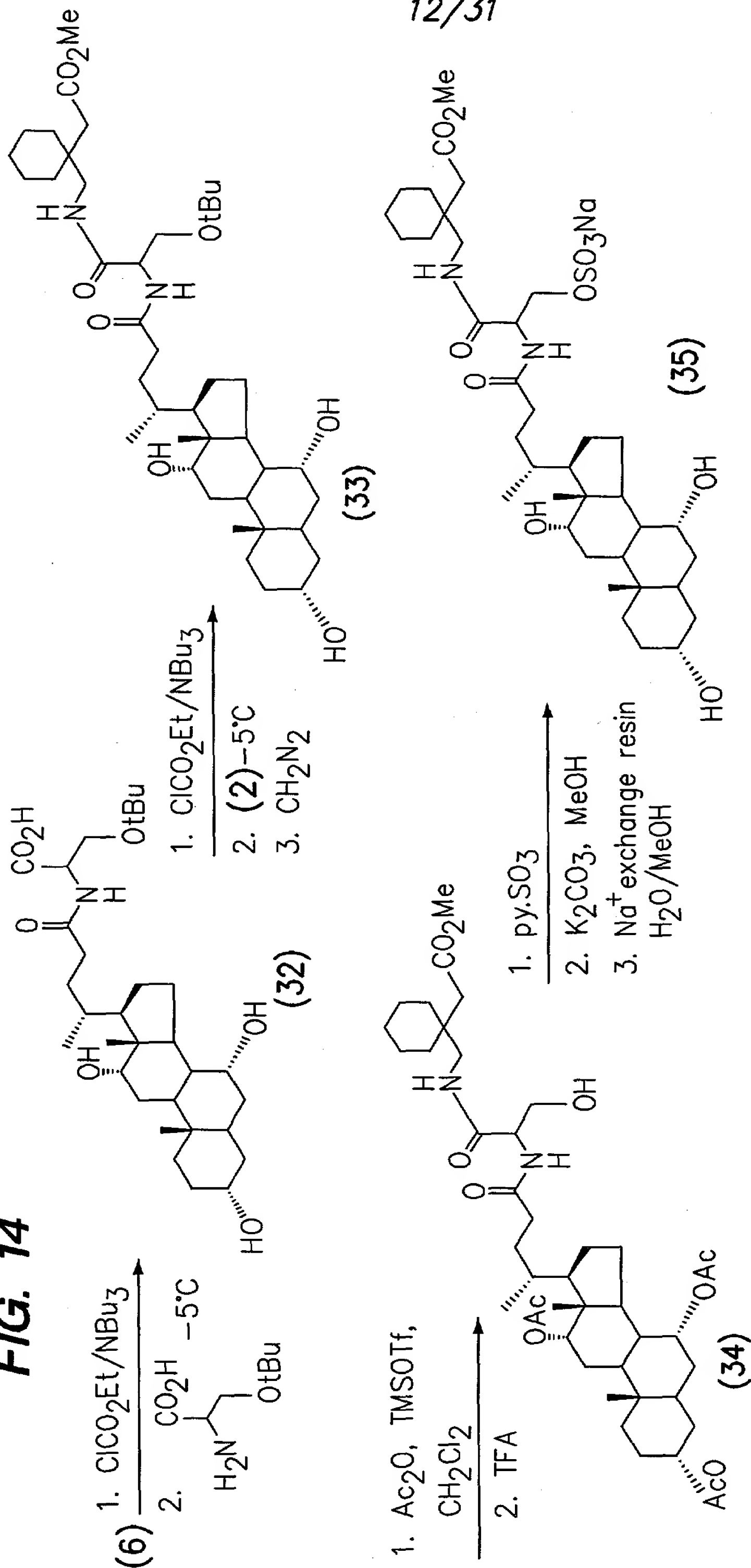


9/31

Agricultural sector		Non-agricultural sector	
Year	Value added	Year	Value added
1970	100	1970	100
1971	105	1971	105
1972	110	1972	110
1973	115	1973	115
1974	120	1974	120
1975	125	1975	125
1976	130	1976	130
1977	135	1977	135
1978	140	1978	140
1979	145	1979	145
1980	150	1980	150
1981	155	1981	155
1982	160	1982	160
1983	165	1983	165
1984	170	1984	170
1985	175	1985	175
1986	180	1986	180
1987	185	1987	185
1988	190	1988	190
1989	195	1989	195
1990	200	1990	200
1991	205	1991	205
1992	210	1992	210
1993	215	1993	215
1994	220	1994	220
1995	225	1995	225
1996	230	1996	230
1997	235	1997	235
1998	240	1998	240
1999	245	1999	245
2000	250	2000	250
2001	255	2001	255
2002	260	2002	260
2003	265	2003	265
2004	270	2004	270
2005	275	2005	275
2006	280	2006	280
2007	285	2007	285
2008	290	2008	290
2009	295	2009	295
2010	300	2010	300
2011	305	2011	305
2012	310	2012	310
2013	315	2013	315
2014	320	2014	320
2015	325	2015	325
2016	330	2016	330
2017	335	2017	335
2018	340	2018	340
2019	345	2019	345
2020	350	2020	350



FIG. 14



12/31

14/31

FIG. 16

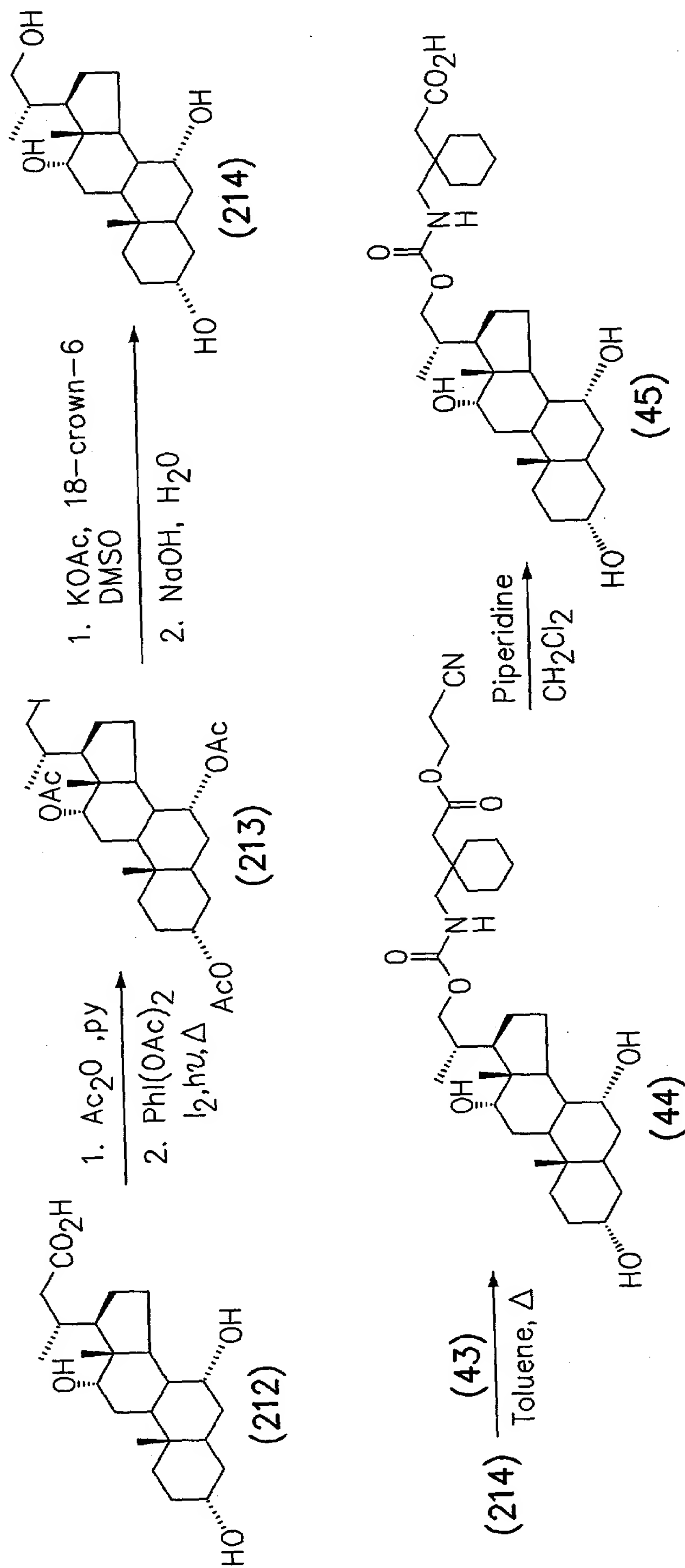
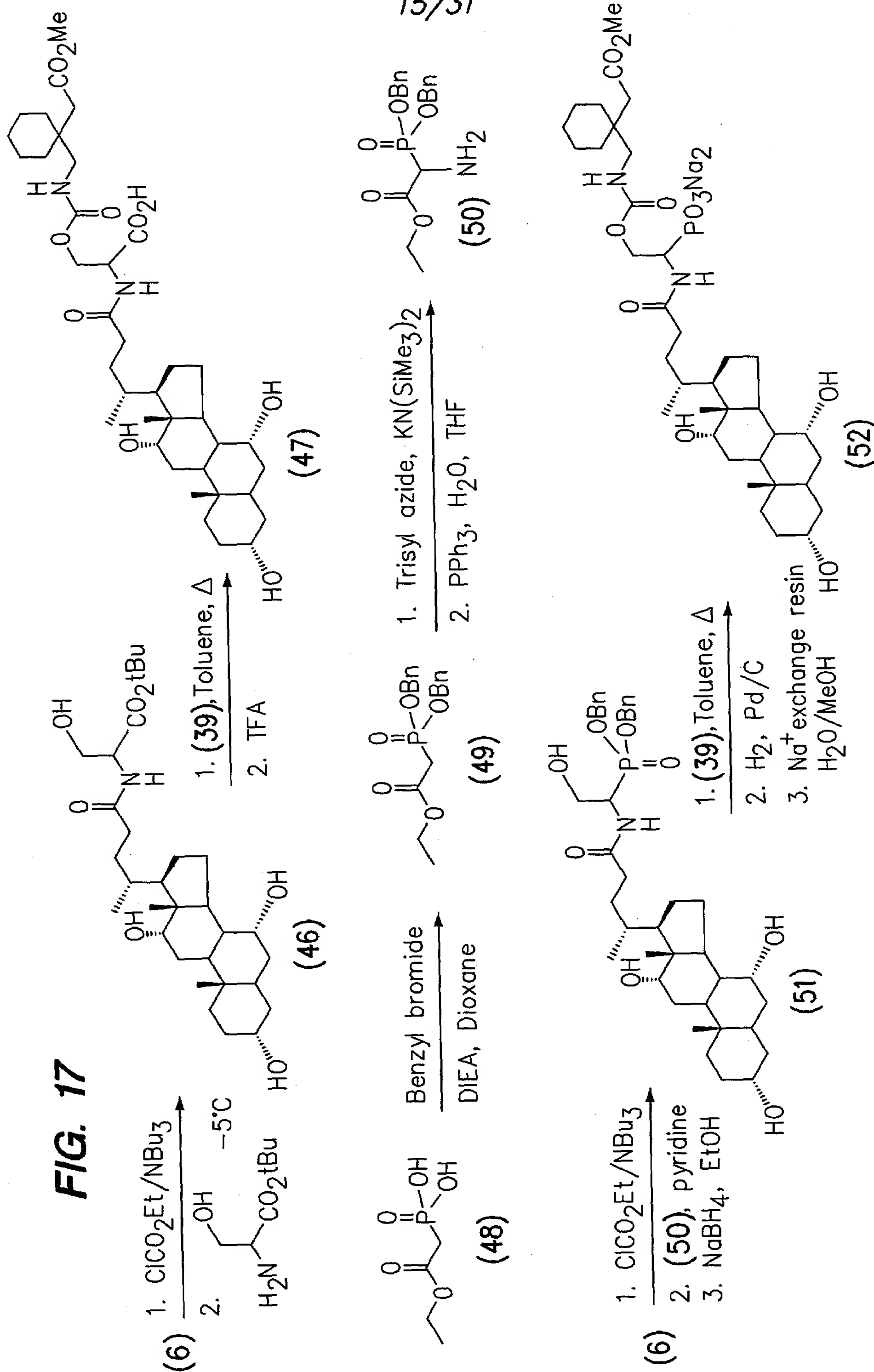


FIG. 17



(27) $\xrightarrow[2. \text{NaBH}_4, \text{EtOH}]{1. \text{ClCO}_2\text{Et}/\text{NBu}_3}$

1. (39), Toluene, Δ
2. TFA
3. 30% H_2O_2 , 2% H_2SO_4
4. Na^+ exchange resin
 $\text{H}_2\text{O}/\text{MeOH}$

(54)

(55)

17/31

FIG. 19

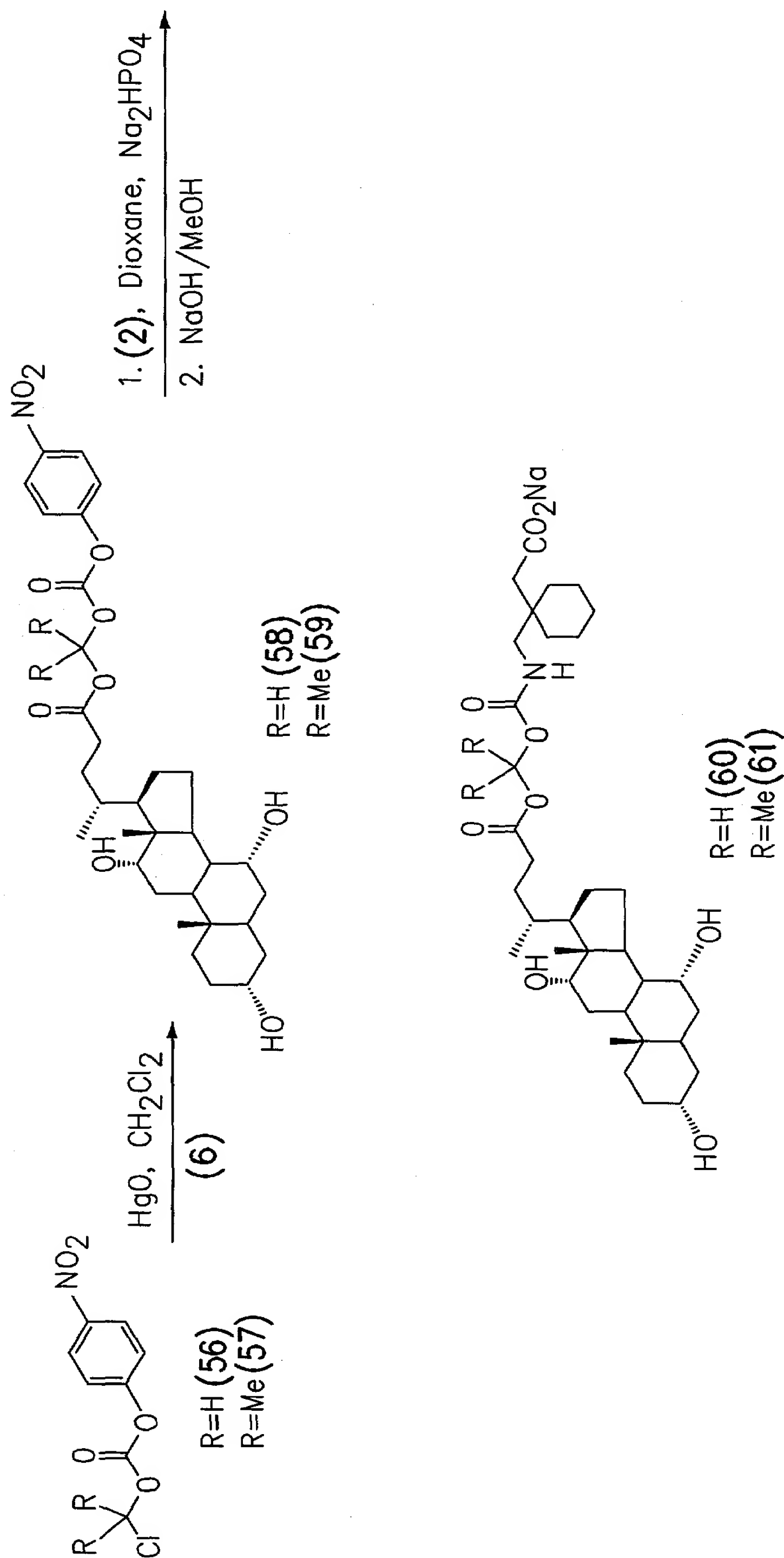


FIG. 20

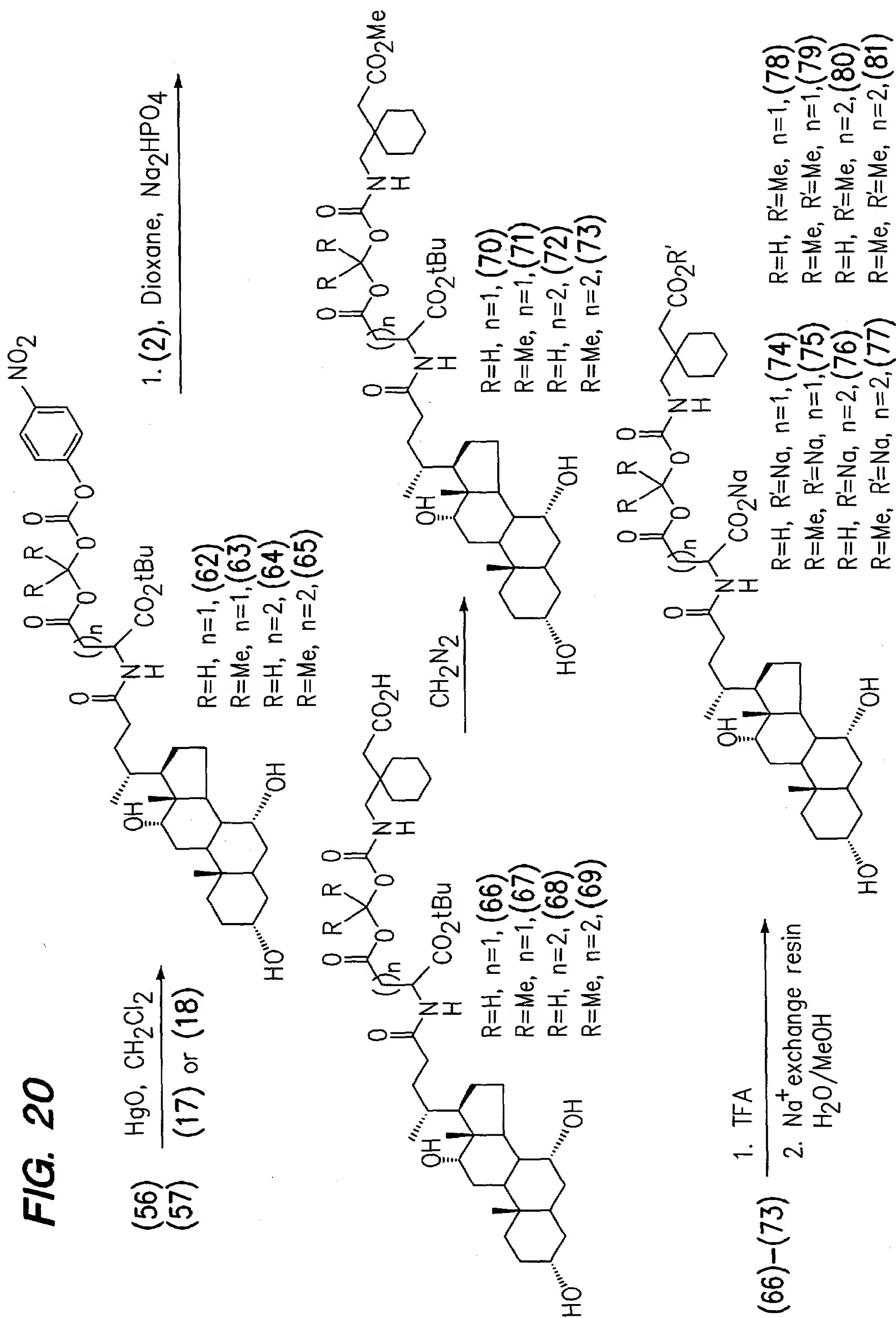
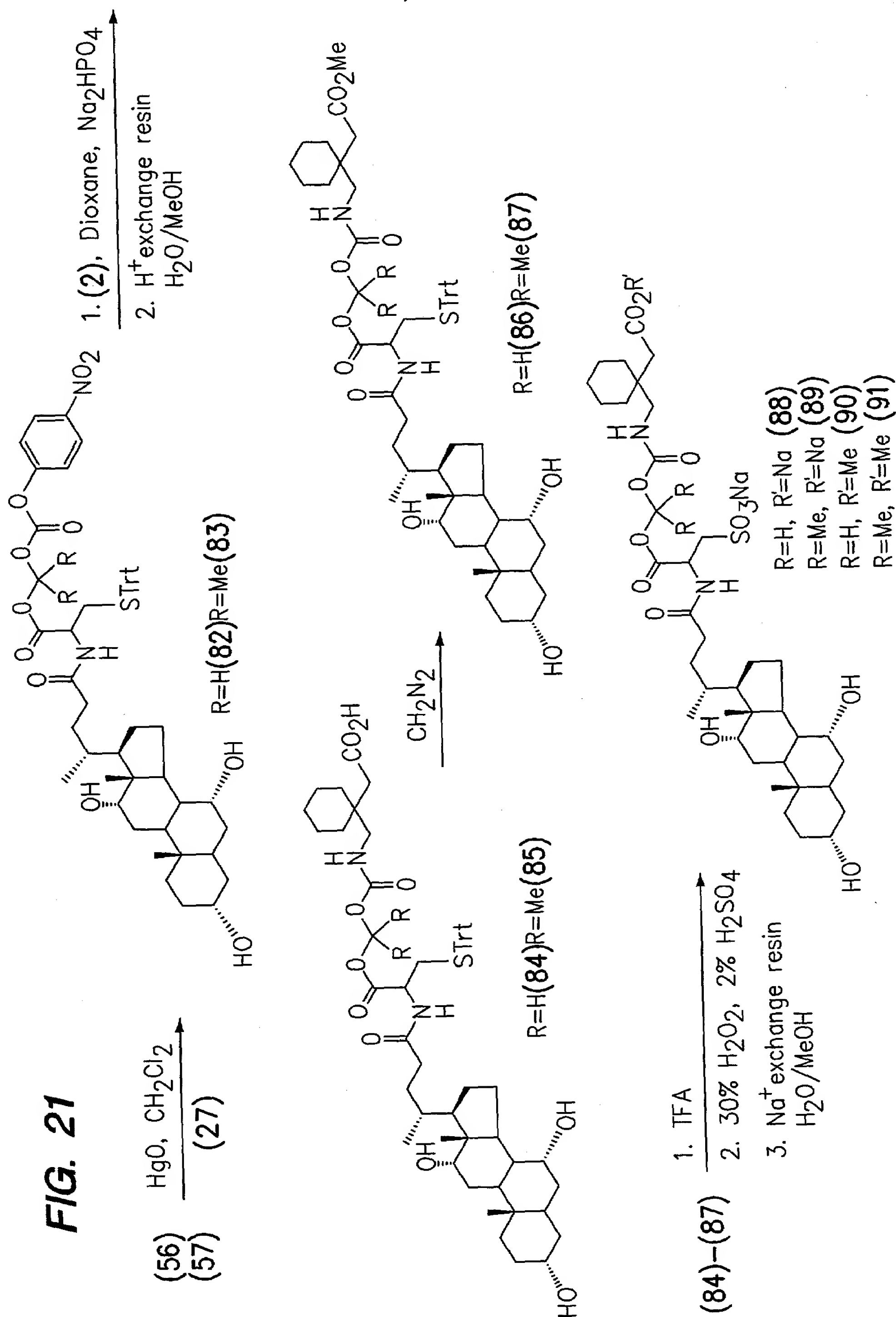
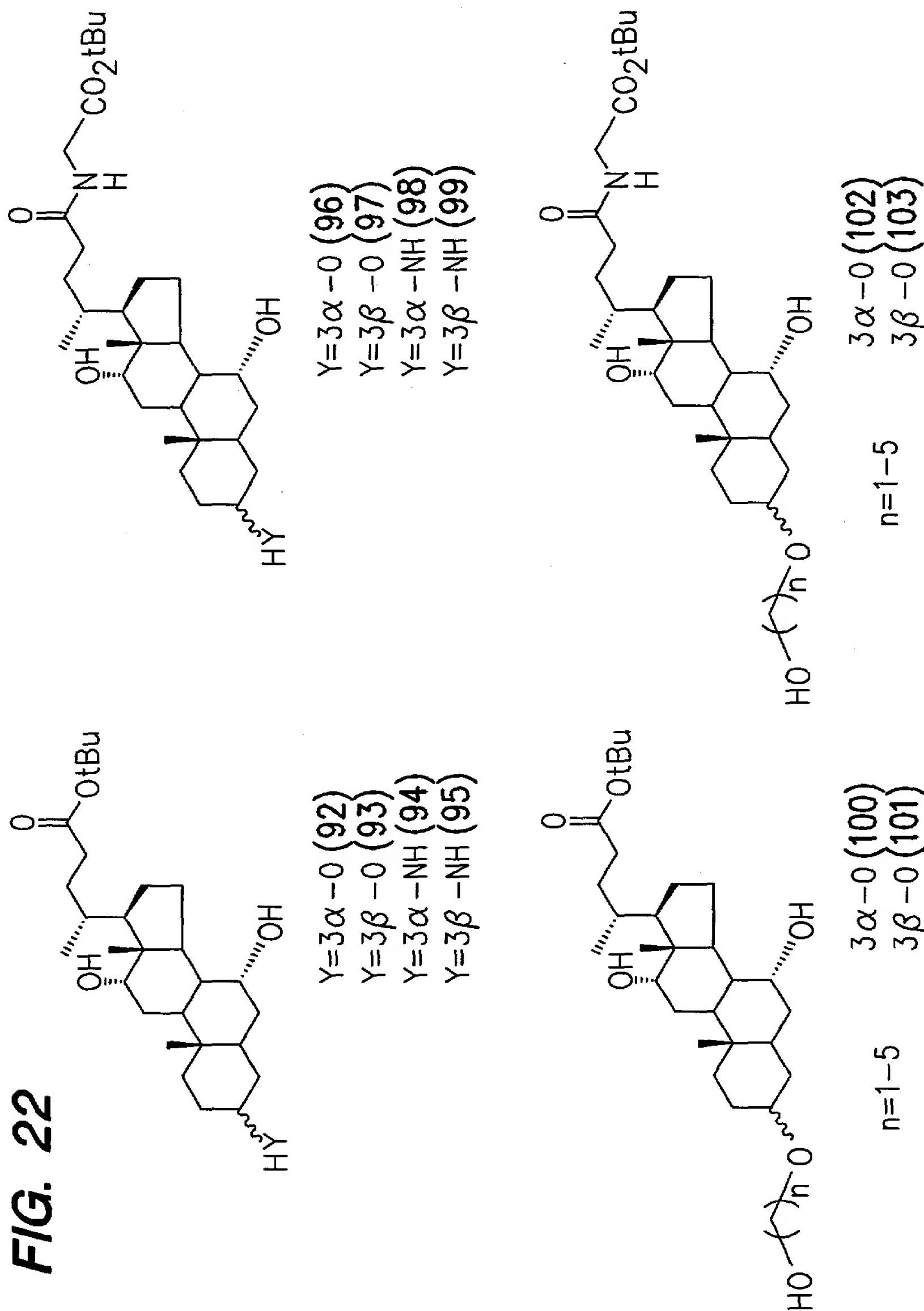


FIG. 21



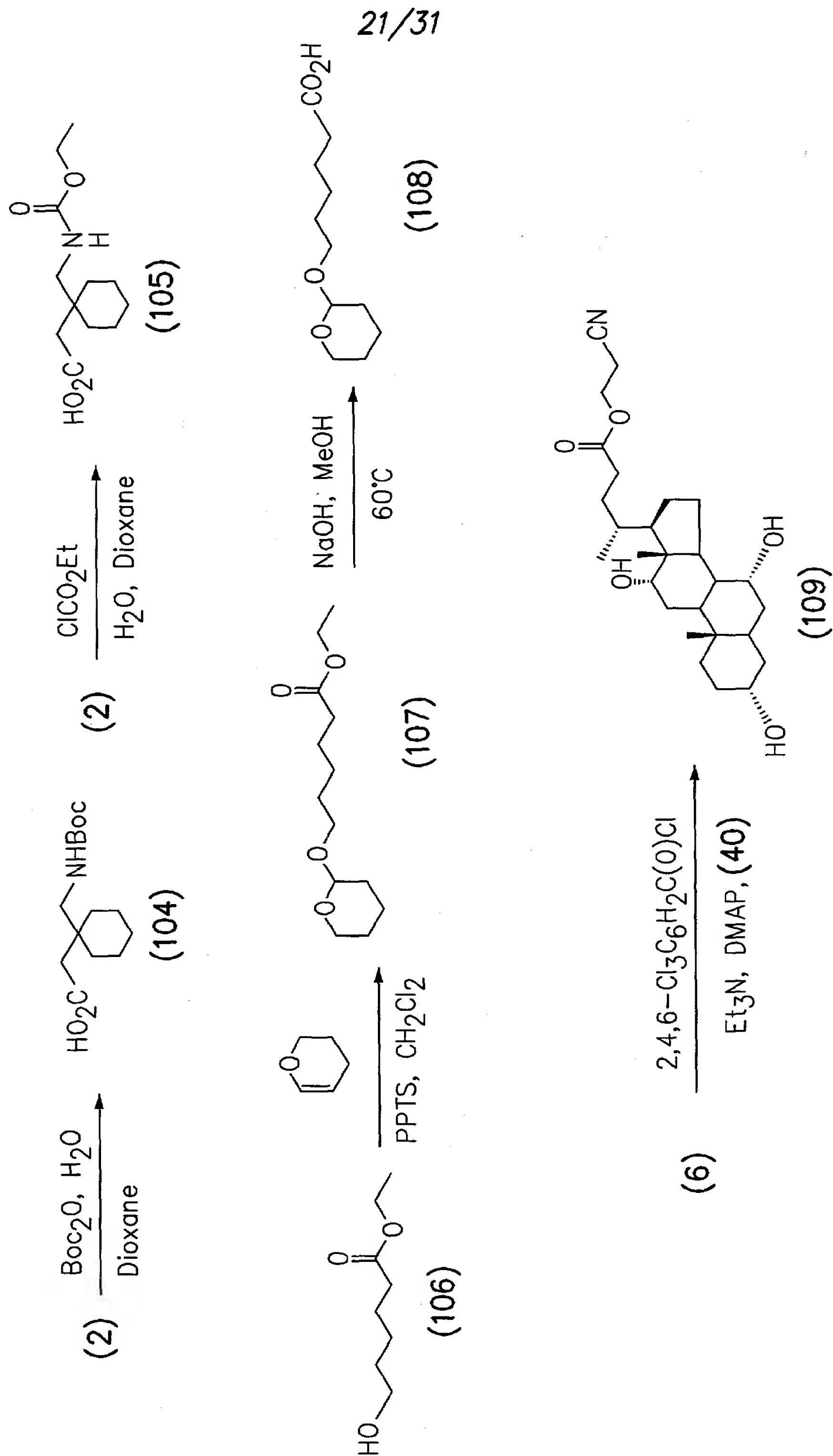
20/31

FIG. 22



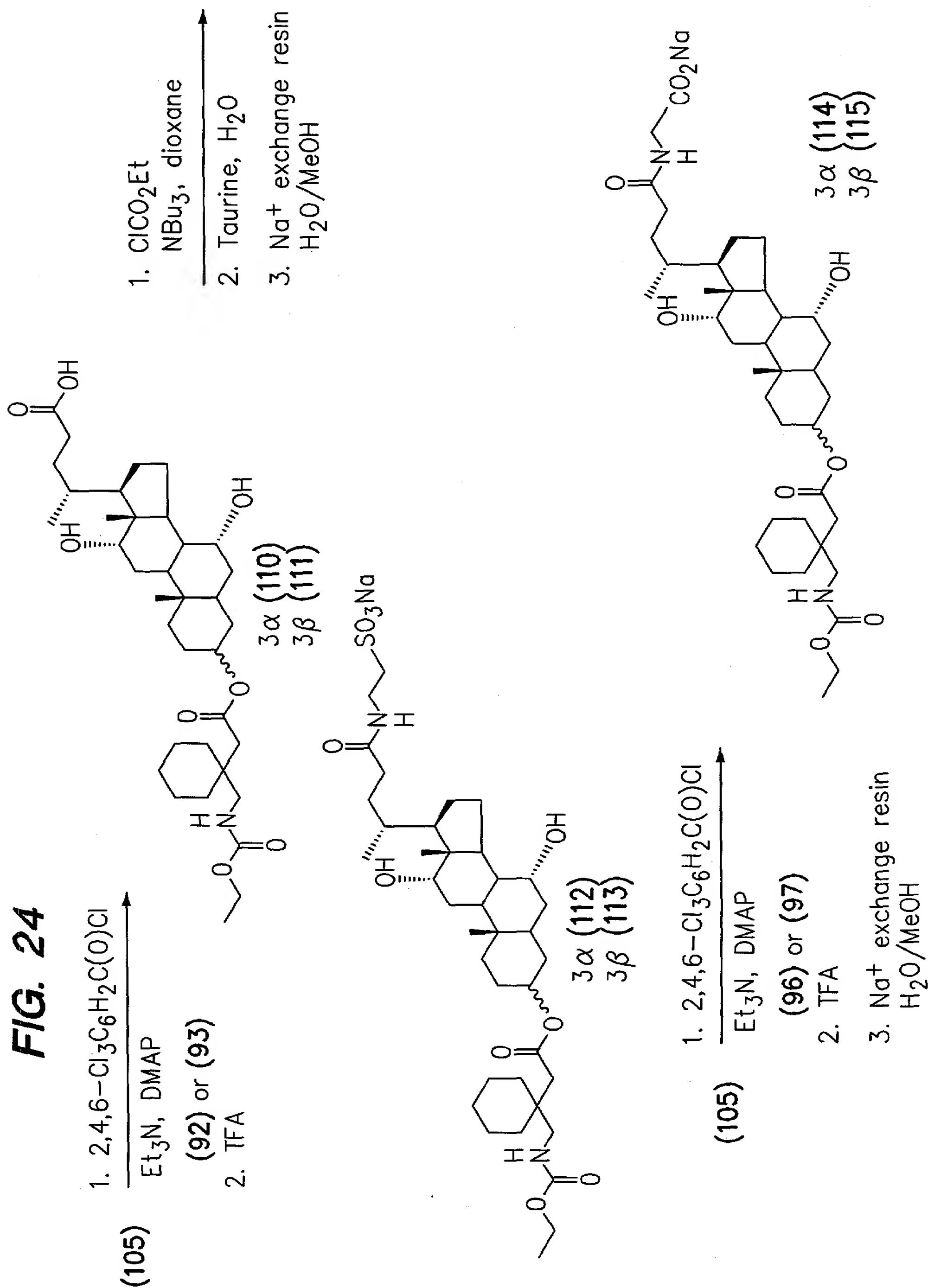
Compounds (92)-(103) prepared following methods described in co-pending application "Bile Acid-Derived Compounds for Enhancing Oral Absorption and Systemic Bioavailability of Drugs" assigned to XenoPort, Inc.

FIG. 23



22/31

FIG. 24



23/31

FIG. 25

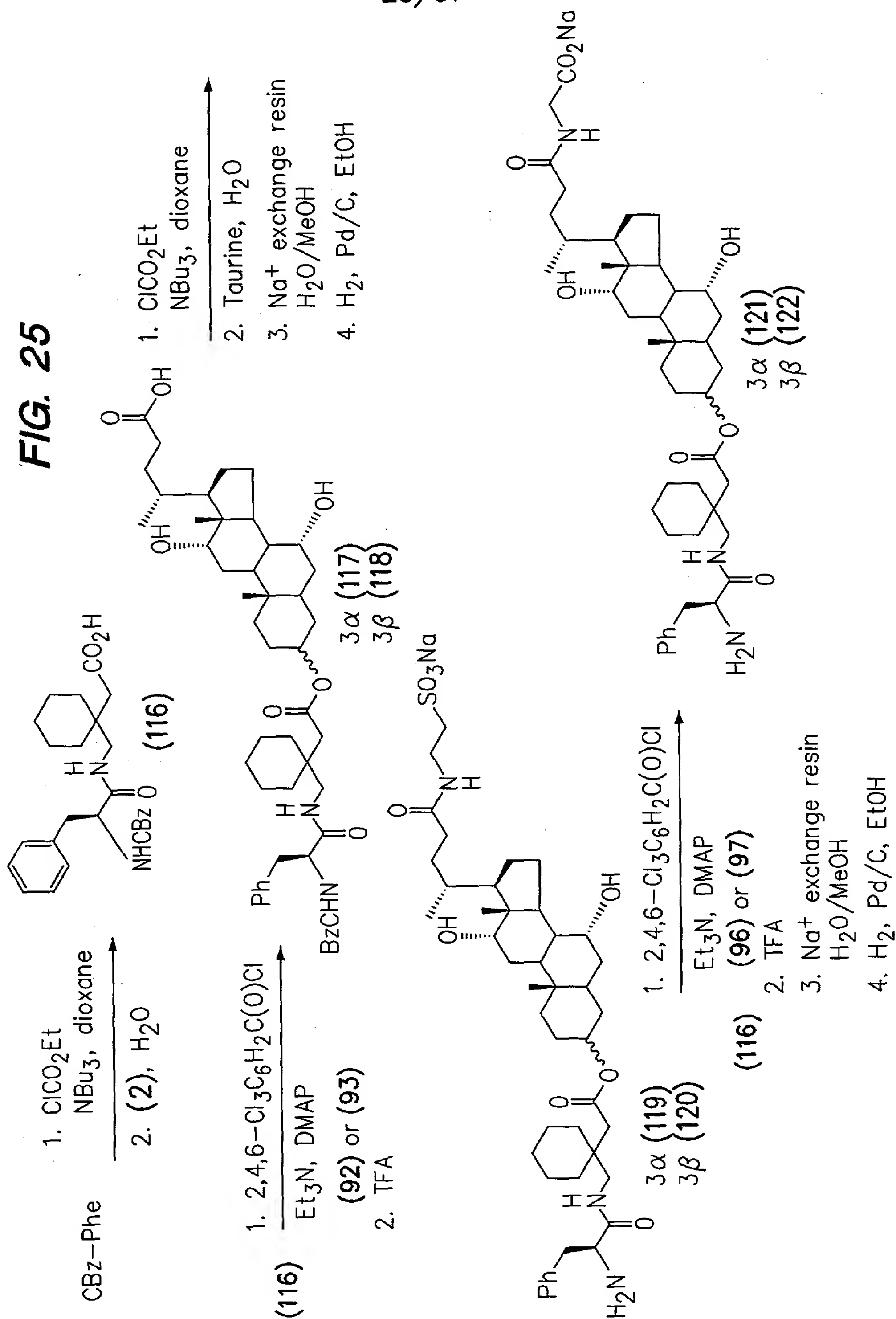
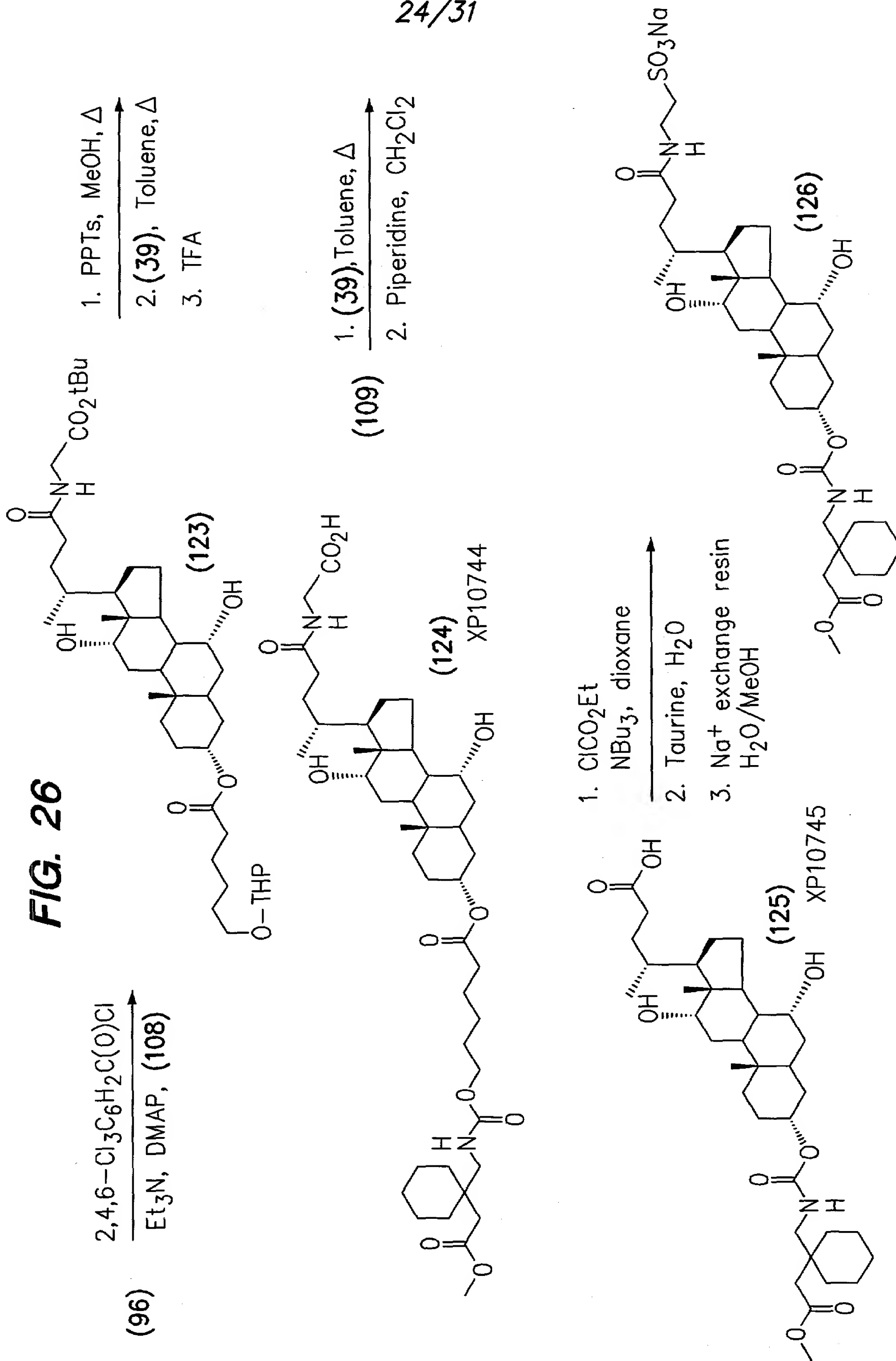
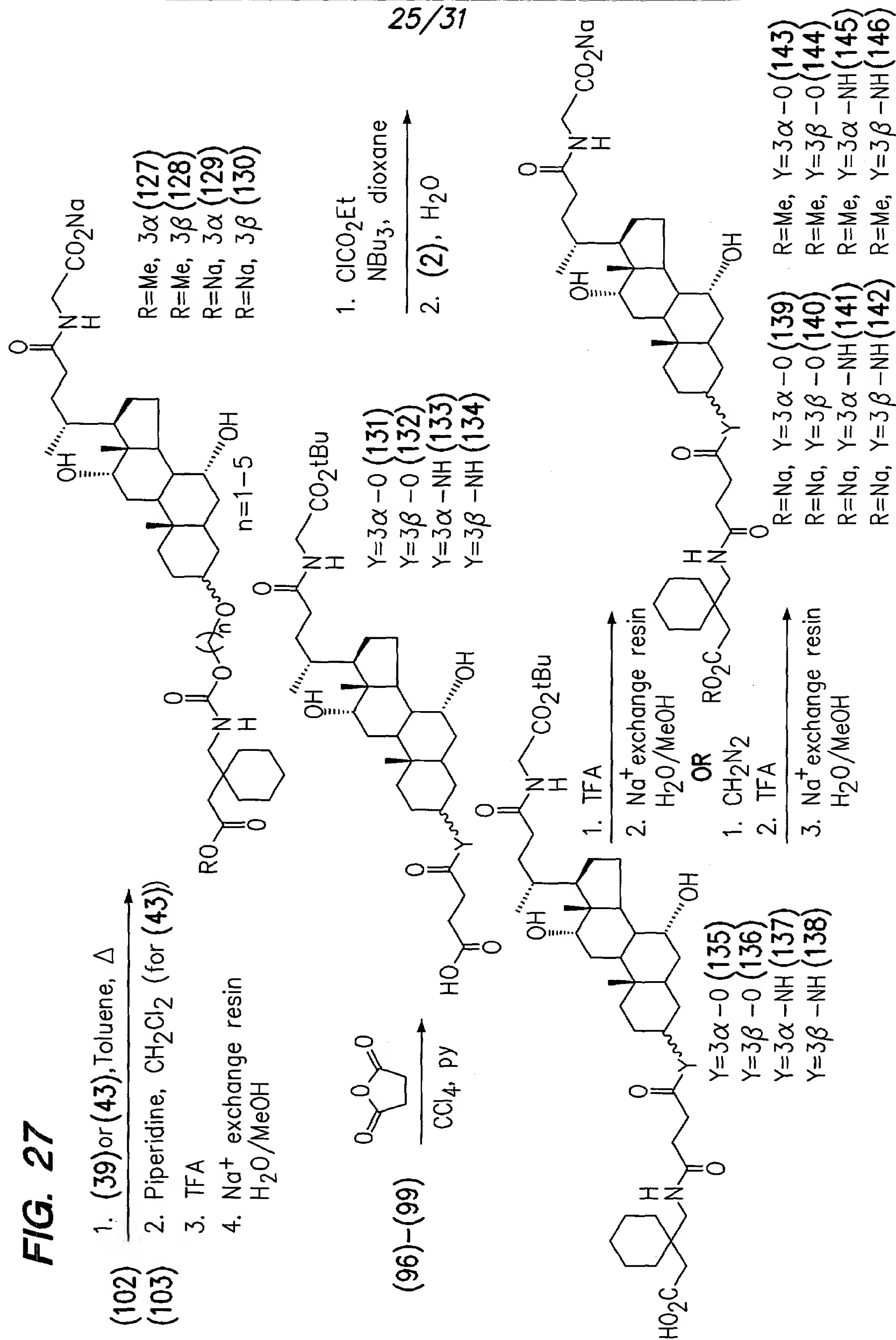


FIG. 26



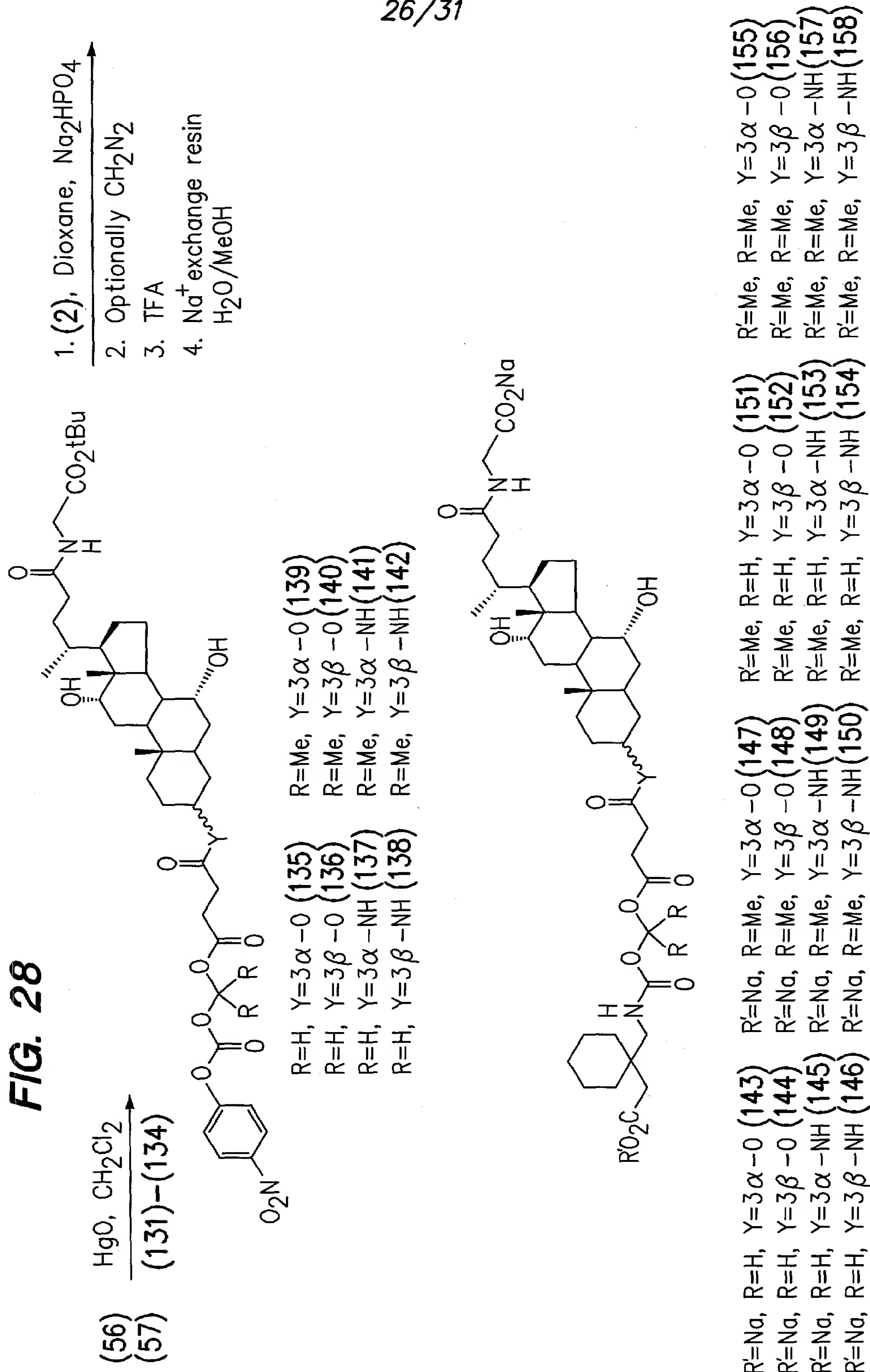
25/31

FIG. 27



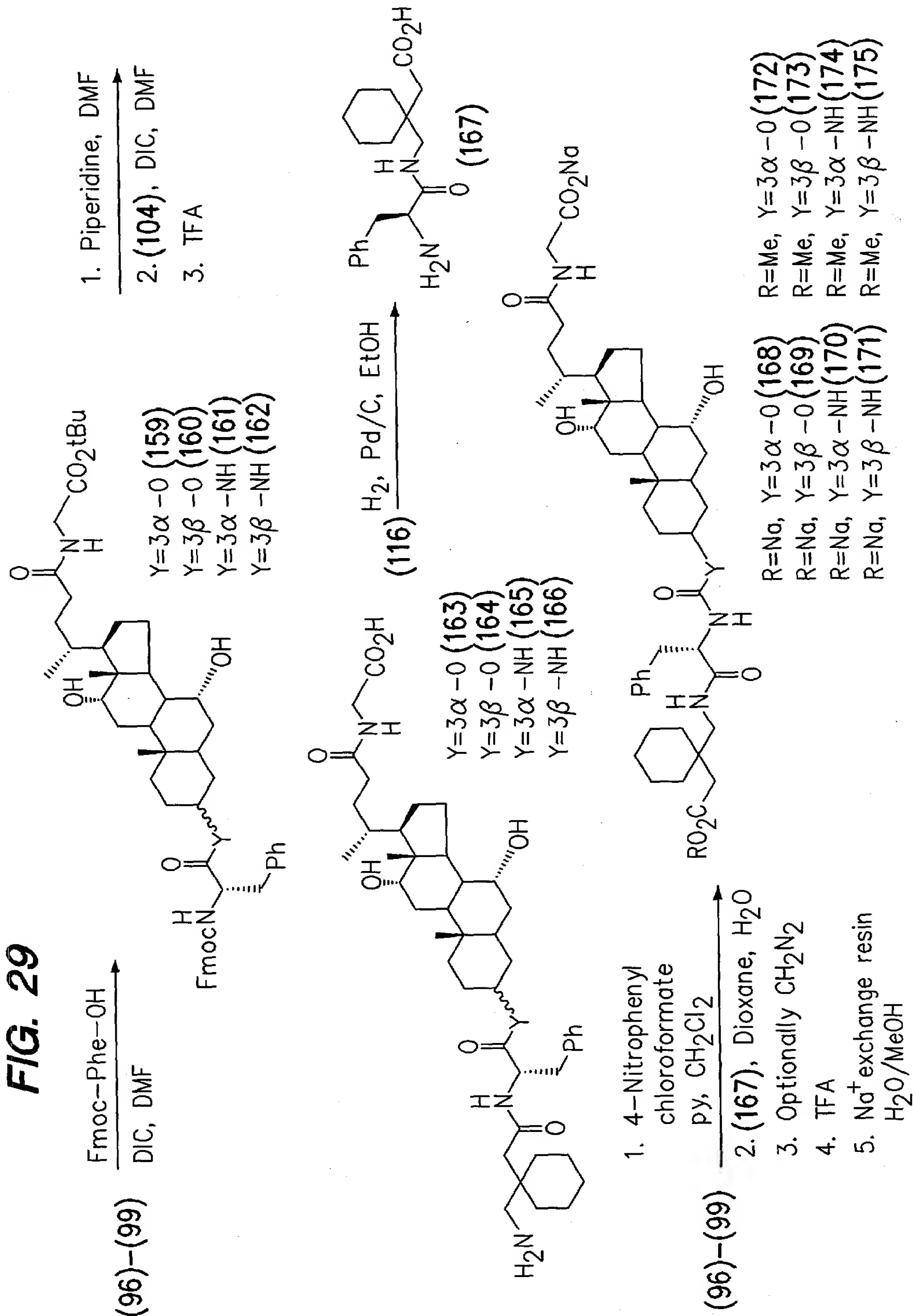
26/31

FIG. 28



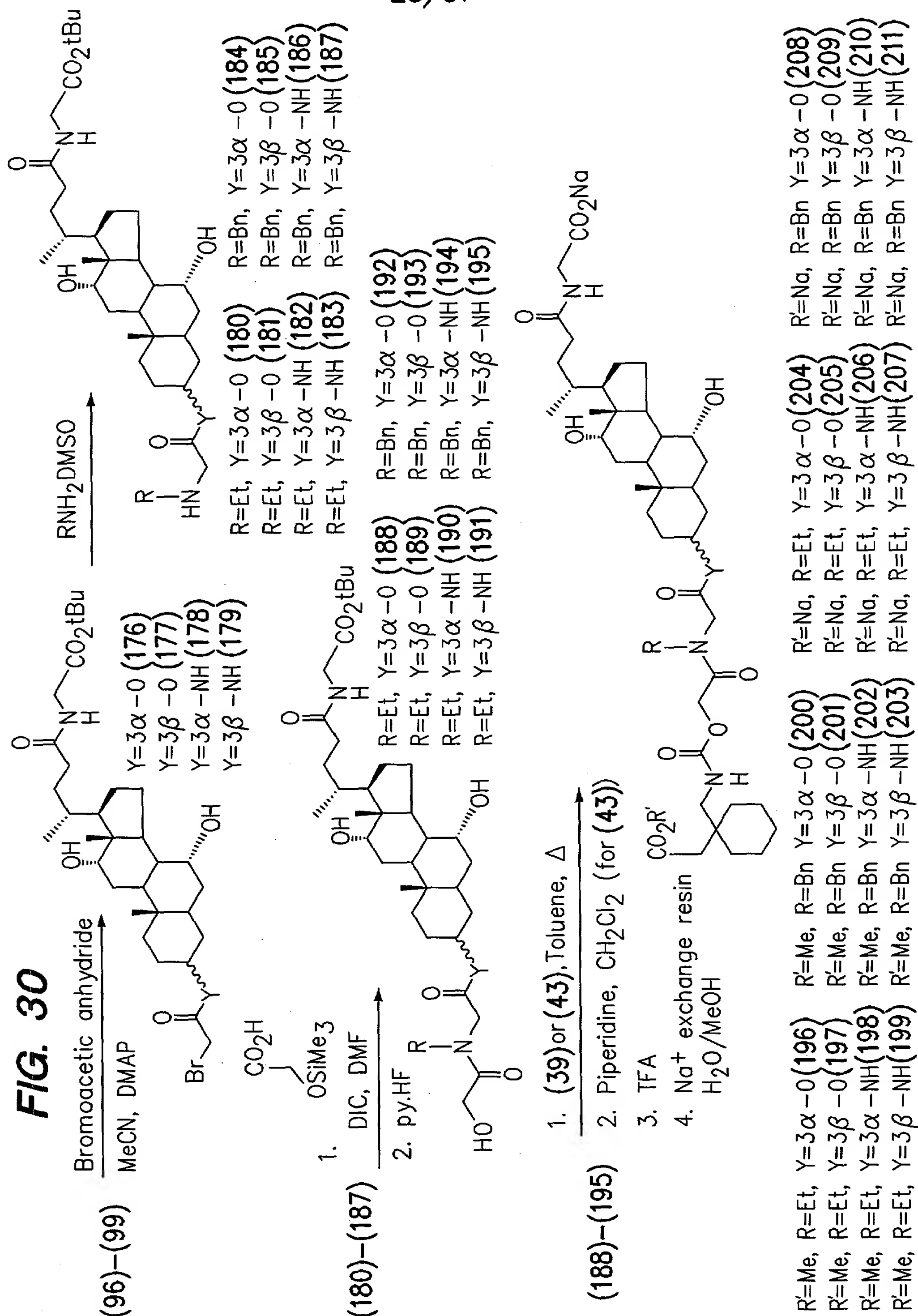
27/31

FIG. 29



28/31

FIG. 30



29/31

FIG. 31

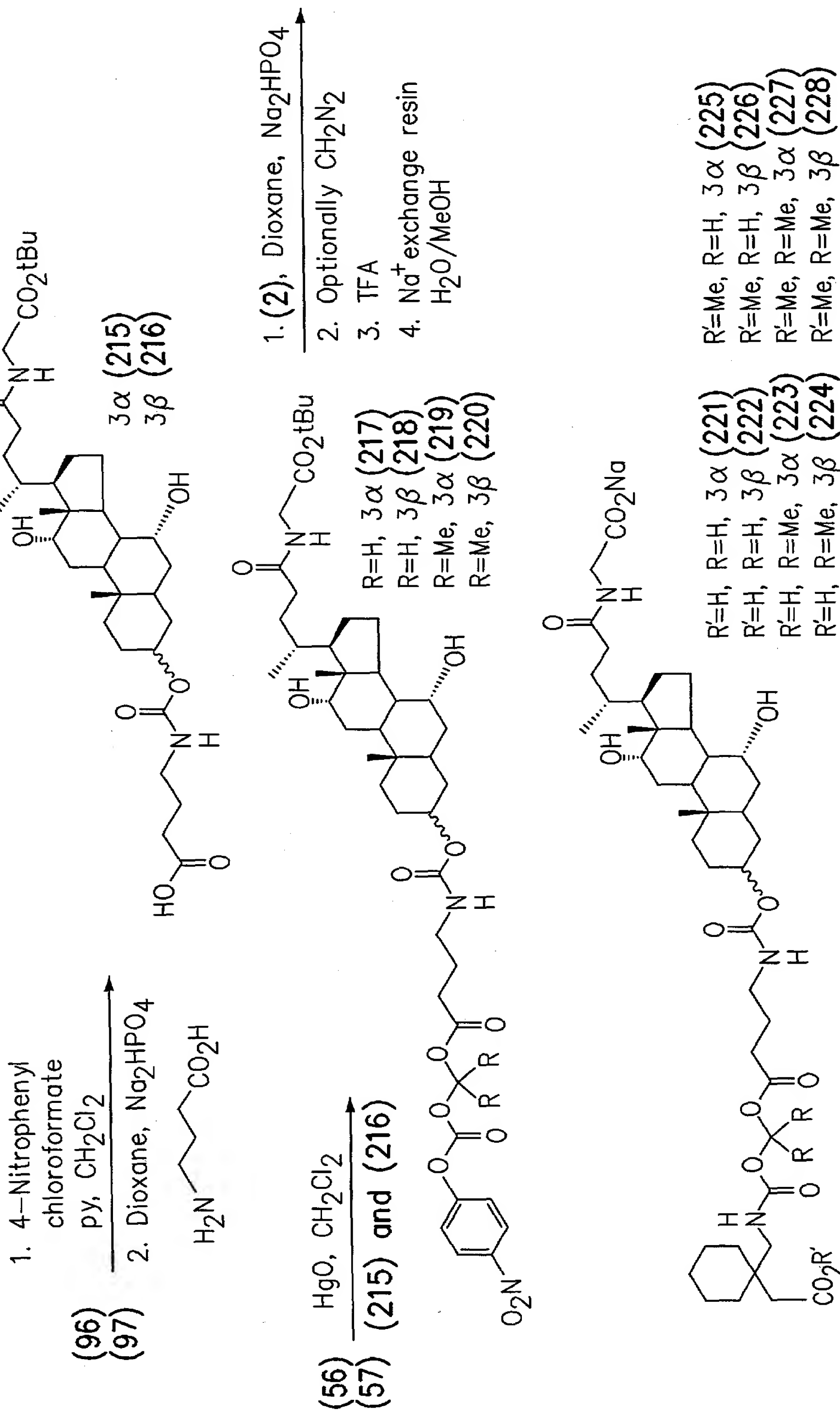


FIG. 32

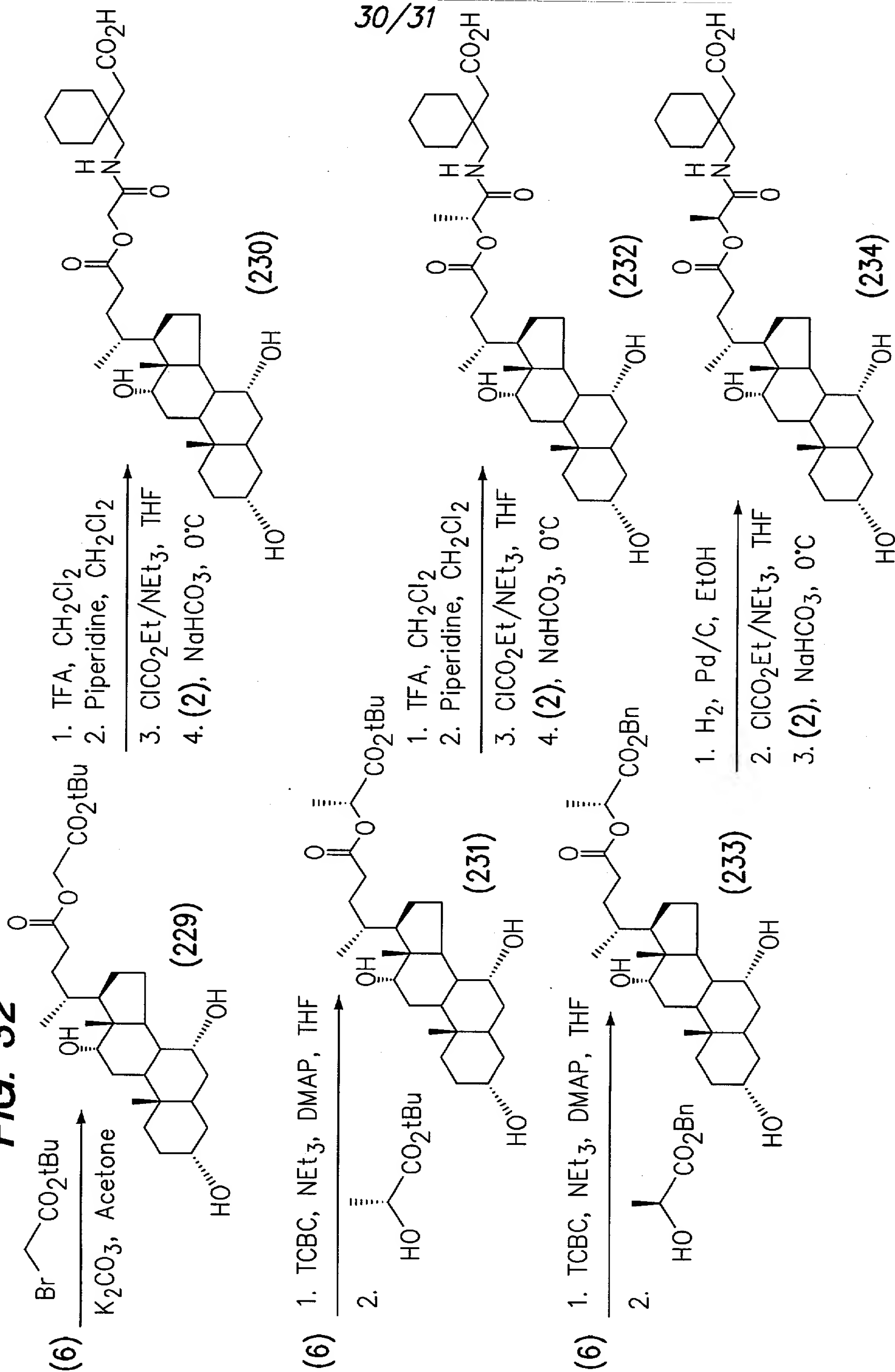


FIG. 33

